UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE AMARIN CORPORATION PLC SECURITIES LITIGATION	Civil Action No. 3:19-cv-06601 Hon. Brian R. Martinotti **CLASS ACTION**

LEAD PLAINTIFFS' AMENDED CLASS ACTION COMPLAINT AND DEMAND FOR JURY TRIAL

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TABLE OF DEFINED TERMS & ABBREVIATIONS

TERM	DEFINITION
ADS	American Depository Share
Advisory Committee	United States Food and Drug Administration's Endocrinologic and Metabolic Drugs Advisory Committee
Advisory Committee Meeting	October 16, 2013 meeting of the United States Food and Drug Administration's Endocrinologic and Metabolic Drugs Advisory Committee
AHA	American Heart Association
AHA Conference	2018 Scientific Sessions of the American Heart Association held on November 10-12, 2018
Amarin	Amarin Corporation, plc and its subsidiaries
Amarin Briefing Document or **Amarin Br. Doc.**	Amarin Pharms. Ireland, Ltd., *Briefing Document for the Endocrinologic and Metabolic Drugs Advisory Committee Meeting* (2013)
Apo B	Apolipoprotein B-100 molecule
CEO	Chief Executive Officer
Class Period	September 24, 2018 through and including November 9, 2018
CMO	Chief Medical Officer
CRL	Complete Response Letter
CSO	Chief Scientific Officer
EPA	Eicosapentaenoic Acid
Exchange Act	Securities Exchange Act of 1934, 15 U.S.C. § 78a *et seq.*
FDA	United States Food and Drug Administration
FDA Briefing Document or **FDA Br. Doc.**	Mary Dunne Roberts, MD, U.S. Food & Drug Admin., *Clinical Review: Endocrinologic and Metabolic Advisory Committee Meeting October 16, 2013* (2013)

TABLE OF DEFINED TERMS & ABBREVIATIONS

TERM	DEFINITION
Forbes Article	Matthew Herper, *Amarin's Fish-Oil-Derived Drug Shows Great Promise—With Big Caveats*, Forbes Healthcare (Nov. 10, 2018), https://www.forbes.com/sites/matthewherper/2018/11/10/fish-oil-derived-drug-shows-great-promise--with-big-caveats/#2e715e0f3291
Granowitz	Craig Granowitz, MD, PhD, Amarin's Chief Medical Officer since January 2016
HDL	High Density Lipoprotein
HDL-C	High Density Lipoprotein Cholesterol
HsCRP	High Sensitivity C-Reactive Protein
Individual Defendants	John F. Thero, Steven Ketchum, Craig Granowitz, and Joseph S. Zakrzewski
Ketchum	Steven Ketchum, PhD, Amarin's President of Research and Development since February 2012 and CSO since January 2016
LDL	Low Density Lipoprotein
LDL-C	Low Density Lipoprotein Cholesterol
MACE	Major Adverse Cardiac Events
NDA	New Drug Application
NEJM Article	Deepak L. Bhatt, M.D., M.P.H., et al., *Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia*, 380 N. Engl. J. Med. 11 (2018)
Officer Defendants	John F. Thero, Steven Ketchum, and Craig Granowitz
SEC	United States Securities and Exchange Commission
***Sklar* Action**	Action filed by Steven Sklar captioned *In re Amarin Corporation PLC, Securities Litigation*, 3:13-cv-06663-FLW-TJB (D. N.J. November 1, 2013)

TABLE OF DEFINED TERMS & ABBREVIATIONS

TERM	DEFINITION
sNDA	Supplemental New Drug Application
Thero	John F. Thero, Amarin's President since 2010 and CEO since January 2014
Zakrzewski	Joseph S. Zakrzewski, Amarin's President and CEO from November 2010 to December 2013, and a Director on Amarin's board since January 2010

GLOSSARY

TERM	DEFINITION
Apo B	Apolipoprotein B-100 molecule, a protein that is involved in the metabolism of lipids and the main protein constituent of LDL.
Atherosclerosis	The process of plaque buildup or "calcification" of the arteries.
Atherosclerotic Cardiovascular Disease	Plaque buildup in the arteries, disrupting the flow of blood in the body.
Baseline	The measurement of a condition in a patient before treatment is administered.
Biomarkers	A broad subcategory of medical signs—that is, objective indications of medical state observed from outside the patient—which can be measured accurately and reproducibly.
Coronary Revascularization	Heart surgery, such as bypass surgery or placement of stents.
Cholesterol	Lipids found in the blood that are used to build cells and hormones.
EPA	Eicosapentaenoic Acid, an omega 3 fatty acid.
HDL	High Density Lipoprotein, the lipoprotein which carries cholesterol from the tissues to be disposed of in the liver.
HDL-C	High Density Lipoprotein Cholesterol, the cholesterol found in the HDL lipoprotein.
HsCRP	High Sensitivity C-Reactive Protein, a protein released into the blood by the liver during inflammation, and thus a commonly used clinical marker of general and cardiac-related inflammation.
Hypertriglyceridemia	A condition diagnosed when blood triglyceride levels rise above a threshold value, such as the 90th or 95th percentile, depending upon the patient's age and gender.
Icosapent Ethyl	An ethyl ester of the omega-3 fatty acid Eicosapentaenoic acid, a/k/a Vascepa.

GLOSSARY

TERM	DEFINITION
Indication	The use of a drug to treat a specific disease or condition.
Ischemia	The restriction of blood supply to the tissues of the body.
LDL	Low Density Lipoprotein, the lipoprotein that carries the majority of the cholesterol in circulation in the blood.
LDL-C	Low Density Lipoprotein Cholesterol, the cholesterol found in the LDL lipoprotein.
Lipids	Fatty-like substance found in the blood.
Lipoproteins	Soluble particles made up of lipids and proteins to carry lipids through the blood.
Mechanism of Action	The biochemical process through which a drug produces its effect.
Mixed Dyslipidemia	A condition diagnosed when a patient has abnormally high LDL-C levels combined with at least one other lipid abnormality.
Myocardial Infarction	Heart attack.
Myocardial Ischemia	The restriction of blood flow to the heart, preventing the heart muscle from receiving enough oxygen.
Phase 3 Trial	Trial involving randomized and blind testing of a drug in several hundred to several thousand patients to provide additional safety and efficacy data to support approval of the drug by the FDA.
Primary Endpoint	The main, pre-determined measure of a clinical trial to establish the effectiveness and/or safety features of a drug in order to support approval by the FDA.
Principal Investigator	A principal trial investigator is the physician responsible for supervising the conduct of a clinical trial in compliance with the current protocol, good clinical practices, and all applicable laws.

GLOSSARY

TERM	DEFINITION
Secondary Endpoint	A secondary measure selected to demonstrate additional effects or benefits of a drug, analyzed after the primary endpoint.
Statins	Chemicals which inhibit the primary enzyme responsible for synthesizing cholesterol, HMG-CoA reductase, and the standard of care for reducing LDL-C.
Triglycerides	Lipids found in the blood that store unused calories.
Unstable Angina	Poor blood flow through the arteries due to blood clots.

CHRONOLOGY

DATE	EVENT
Jul. 2008	The Food and Drug Administration ("FDA") meets with Amarin to discuss Amarin's plans to develop Vascepa (then "AMR101") for the treatment of hypertriglyceridemia. The FDA and Amarin agree upon a Phase 3 trial program with three pivotal trials to test Vascepa: the MARINE, ANCHOR, and REDUCE-IT trials. ¶36.
Dec. 2009	Patient enrollment begins for Amarin's Phase 3 MARINE trial. ¶37.
Jan. 2010	Amarin initiates its Phase 3 ANCHOR trial. ¶42.
Nov. 29, 2010	Amarin announces that the MARINE trial has met its primary endpoints for median reductions in triglyceride levels. ¶39.
Apr. 18, 2011	Amarin reports top-line results for the ANCHOR trial, stating that the primary endpoint for the reduction of triglyceride levels was met. ¶43.
Sept. 2011	Amarin submits a New Drug Application ("NDA") to the FDA requesting approval to market and sell Vascepa for the MARINE indication, *i.e.*, the reduction of triglyceride levels for patients with very high triglycerides (>500 mg/dL). ¶40.
Sept. 2011	According to a class action complaint filed in 2014, a senior director of clinical research and medical affairs at Amarin first expresses concern to key Amarin employees, including then-CEO and current Chairman of the Board Joseph Zakrzewski, that the mineral oil used in Amarin's phase 3 trials was not inert. ¶66.
Nov. 2011	Amarin initiates its third and largest Phase 3 REDUCE-IT trial. The trial is intended to evaluate whether Vascepa, combined with statin therapy, will be superior to statin therapy alone when used to reduce long-term cardiovascular events in high-risk patients with mixed dyslipidemia. ¶44.
Jul. 26, 2012	Amarin announces that the FDA approved Vascepa for the MARINE indication. ¶41.
Jan. 2013	Amarin begins marketing Vascepa under the MARINE indication. ¶41.
Feb. 21, 2013	Amarin files a supplemental NDA ("sNDA") with the FDA for expanded approval of Vascepa based upon the ANCHOR indication, *i.e.*, treatment in combination with a statin to reduce triglyceride, non-HDL-C, Apo B, LDL-C, TC, and VLDL-C in adult patients with mixed dyslipidemia and coronary heart disease or a coronary heart disease equivalent. ¶49.

CHRONOLOGY

DATE	EVENT
Oct. 11, 2013	The FDA publishes a Briefing Document prior to the meeting of the Endocrinologic and Metabolic Drugs Advisory Committee which provides analysis of Amarin's sNDA based upon the ANCHOR trial. The FDA Briefing Document notes that the mineral oil placebo may not have been inert. ¶¶49-51.
Oct. 16, 2013	The FDA holds a meeting of the Endocrinologic and Metabolic Drugs Advisory Committee to discuss approval of the expanded ANCHOR indication. Potential problems with the placebo arm of the ANCHOR trial are discussed at the meeting. ¶¶54-59.
Nov. 1, 2013	The *Sklar* securities class action case is filed in the United States District Court for the District of New Jersey alleging violations of Sections 10(b) and 20(a) of the Exchange Act and Rule 10b-5 in relation to Amarin's statements surrounding the ANCHOR trial and FDA approval prospects. ¶64.
Sept. 19, 2014	The *Sklar* action is amended to include allegations concerning Amarin's use of mineral oil as a placebo and its impact distorting trial results. Thero and Ketchum are added as defendants. ¶65.
Apr. 27, 2015	The FDA provides a Complete Response Letter to Amarin denying approval of the sNDA for the broader use of Vascepa based upon the results of the ANCHOR trial. ¶67.
Mar. 2018	Amarin completes the last study visits for the Company's REDUCE-IT trial. ¶69.
Sept. 12, 2018	Amarin announces that the REDUCE-IT trial results have been accepted for presentation at the 2018 Scientific Sessions of American Heart Association ("AHA") on November 10, 2018 (the "AHA Conference"). ¶70.
Sept. 24, 2018	**Class Period Begins** – Amarin issues a press release announcing the REDUCE-IT trial's results, claiming that the study had met its primary endpoint and demonstrated a 25% relative risk reduction for major cardiovascular events. ¶71. Amarin executives reiterate the same purported results during a conference call, ¶72, and during a CNBC appearance that same day. ¶74.
Oct. 3, 2018	Defendant Thero touts the REDUCE-IT trial's 25% relative risk reduction results at the Cantor Fitzgerald Global Healthcare Conference. ¶78.
Nov. 1, 2018	In a quarterly financial report signed by Thero and on Amarin's Q3 2018 Conference Call, Defendant Thero again touts the REDUCE-IT trial's 25% relative risk reduction results. ¶¶79-82.

CHRONOLOGY

DATE	EVENT
Nov. 9, 2018	**Class Period Ends** – the last trading day before Amarin presents more complete results at the AHA Conference. ¶¶84-92, 168.
Nov. 10, 2018	At the AHA Conference and through a simultaneous publication in the New England Journal of Medicine, more detailed REDUCE-IT trial data reveals that the mineral oil used in the REDUCE-IT placebo arm may not have been inert and that the mechanism of action responsible for the benefit seen in the Vascepa arm is not known, thereby calling into question the true effectiveness of Vascepa. ¶¶83, 85-92.
Nov. 10, 2018	In the aftermath of the disclosure of Amarin's more complete REDUCE-IT trial results, news articles are published criticizing the results. For example, Matthew Herper publishes the article *Amarin's Fish-Oil-Derived Drug Shows Great Promise—With Big Caveats* in Forbes. The article cites several cardiologists expressing newfound criticism of the REDUCE-IT results, including concerns that the placebo used in the trial was not inert and the mechanism by which Vascepa functions remains unknown. ¶¶93-102.
Nov. 12-13, 2018	The Company's shares decline by 27% from $21.05 to $15.38 per share over the next two trading days. ¶105.

Plaintiffs Dan Kotecki and Gaetano Cecchini as Trustee of the Gaetano Cecchini Living Trust (together "**Lead Plaintiffs**" or "**Plaintiffs**") bring claims arising under Sections 10(b) and 20(a) of the Securities and Exchange Act of 1934, 15 U.S.C. § 78 *et seq.* (the "**Exchange Act**"), individually and on behalf of all persons and entities who purchased or otherwise acquired Amarin ("**Amarin**" or the "**Company**") American Depository Shares ("**ADS's**" or "**shares**") between September 24, 2018, and November 9, 2018, inclusive (the "**Class Period**"), and who were damaged thereby. Plaintiffs' allegations are based on personal knowledge as to themselves and their actions, and upon information and belief as to all other matters. Plaintiffs' information and belief is based on, among other things, the investigation of their undersigned counsel (including the review of certain press releases, analyst reports, media reports, conference call transcripts, and filings with the United States Securities and Exchange Commission ("**SEC**")). Plaintiffs' investigation into the factual allegations contained herein is continuing, and many of the facts related to Plaintiffs' allegations are known only by the Defendants named herein, or are exclusively within their custody or control. Plaintiffs believe that substantial additional evidentiary support will exist for the allegations set forth herein after a reasonable opportunity for discovery.

I. NATURE AND SUMMARY OF THE ACTION

1. Amarin is a pharmaceutical company traded on the NASDAQ Global Market under the ticker symbol AMRN. Since 2008, Amarin has been singularly focused on testing and marketing one drug: Vascepa® (a/k/a icosapent ethyl) ("**Vascepa**"), which is comprised of an omega-3 fatty acid derived from fish oil. The drug is intended to treat heart disease.

2. Over the past decade, Amarin has undertaken three trials to demonstrate Vascepa's efficacy. The first two trials (known as the MARINE and ANCHOR trials) aimed to

demonstrate that Vascepa would lower patients' triglyceride levels. The third trial (known as the REDUCE-IT trial) was the longest and by far the most expensive; it aimed to show Vascepa would reduce patients' major adverse cardiac events.

3. The REDUCE-IT trial wrapped up in the summer of 2018. While the results showed some potentially positive signs for Vascepa (in the form of improved cardiac outcomes) there were two key aberrations in the data that raised serious questions. First, the placebo used in the trial—mineral oil—did not appear to be acting as a mere placebo. Instead, the people in the control arm of the trial who had ingested mineral oil experienced sizeable increases in their LDL-C cholesterol levels and other negative biomarkers. These increases revealed the mineral oil may have skewed the data on how much Vascepa had reduced cardiac risks. Second, the trial data could not explain how Vascepa was actually reducing negative cardiac events. While the drug was supposed to lower triglycerides, among other things, the trial showed no correlation between lowered triglycerides and reduced cardiac events, requiring speculation about Vascepa's causal mechanism.

4. The importance of both issues for the scientific community, investors, and the public at large were well known to Amarin and its officers and directors. After all, the two preceding trials (MARINE and ANCHOR) had both been specifically designed to show that Vascepa worked to lower triglycerides; and various earlier trials had consistently failed to show that omega-3 mixtures (like that comprising Vascepa) could improve cardiac outcomes. Thus, a question mark as to how Vascepa was working (to the extent it was) entailed likely challenges in convincing physicians to prescribe the drug and could impact prospects for approval by the United States Food and Drug Administration ("**FDA**"). And Amarin had already encountered questions about the use of mineral oil as a placebo after the ANCHOR trial, where the FDA had

expressed concern that the oil was not inert and thus was skewing the trial results, which in turn led to Amarin's share price plummeting and an earlier federal securities fraud lawsuit. Thus, Amarin and its officers and directors knew full well that data showing that the mineral oil may have skewed the REDUCE-IT trial results would be an important part of any discussion about the trial.

5. Amarin decided, however, to publicize the REDUCE-IT trial's apparent success in showing improved cardiac outcomes while keeping both aberrations in the data a secret. The Company held a conference call during which the defendants boasted that the results "significantly exceeded the expectations of even the highest degree" and are "the single, most significant advance in preventative cardiovascular drug therapy since the advent of statin therapy." Also during the conference call, they indicated they reviewed all of the data from the trial, but explained that they were not disclosing additional details until the presentation at the American Heart Association ("**AHA**") conference and publication in a peer-reviewed journal in November. Amarin assured the market, however, that the full "[r]esults were supported by robust demonstrations of efficacy across multiple secondary endpoints[,]" and was an "overall robust study result." Analysts and the market were thrilled with this announcement, driving Amarin's share price up from a close of $2.99 per share on September 23, 2018, to $13.00 per share on September 25, 2018—an increase of 433%.

6. With Amarin's shares inflated, several of Amarin's top officers seized on the opportunity to sell an unprecedented number of shares. Amarin's Chief Executive Officer ("**CEO**"), Chief Scientific Officer ("**CSO**"), Chairman of the Board, General Counsel, and Chief Financial Officer collectively sold approximately 3.5 million shares for total profits of approximately $35 million. Around the same time, Amarin continued touting the "remarkable"

risk reduction observed in the REDUCE-IT trial in conferences and SEC filings, while continuing to conceal the aberrations in the data.

7. When the two problems with the REDUCE-IT trial data were finally disclosed on November 10, 2018, at the AHA conference and in the New England Journal of Medicine, preeminent heart experts immediately voiced concern over the data and its implications. Articles published on November 10th and 11th explained "that it's possible that the placebo was[n't] really a 'placebo,'" that the placebo may have helped overstate Vascepa's "true effect," and that the unexplained causal mechanism could mean the trial results were "a one-off chance finding." As a result, Amarin's stock price shot down over the course of two days, falling from a close of $21.05 per share on Friday November 9, 2018, to a close of $15.38 per share on Tuesday November 13, 2018, a drop of $5.67 per share or 27%, on unusually high volume. Before the stock price had bottomed out, though, Amarin's executives had already offloaded their shares at a handsome profit, leaving ordinary investors like Plaintiffs and Class members to bear the losses.

8. Defendants' fraudulent acts and omissions, which led to the inflation and precipitous decline in the market value of the Company's stock when the truth was revealed, caused Plaintiffs and other Class members to suffer significant damages, which this action seeks to recover.

II. JURISDICTION AND VENUE

9. This Court has jurisdiction and venue over the subject matter of this action pursuant to Section 27 of the Exchange Act, 15 U.S.C. § 78aa and 28 U.S.C. § 1331.

10. Venue is proper in this District pursuant to Section 27 of the Exchange Act, 15 U.S.C. § 78aa, and 28 U.S.C. § 1391(b), (c), and (d). Many of the acts, omissions, and transactions at issue, including the preparation and dissemination of materially false and

misleading statements, occurred in this District. At all relevant times, Amarin's U.S. headquarters were located in this District.

11. In connection with the acts alleged in this Complaint, Defendants used the means and instrumentalities of interstate commerce, including the United States mail, interstate telephone communications, and the facilities of the national securities exchange.

III. THE PARTIES

12. As set forth in a certification previously filed with the Court, Court-appointed Lead Plaintiff Dan Kotecki purchased Amarin ADS's during the Class Period and was damaged thereby.

13. Court-appointed Lead Plaintiff Gaetano Cecchini as Trustee of the Gaetano Cecchini Living Trust purchased Amarin ADS's during the Class Period and was damaged thereby, as set forth in the certification that he previously filed with the Court.

14. Defendant Amarin is a biotechnology company with its headquarters located in Dublin, Ireland and its U.S. office located at 1430 Route 206, Bedminster, New Jersey 07921. Amarin's ADS's are traded under the symbol AMRN on the NASDAQ Global Market, which is an efficient market.

15. Defendant John F. Thero was the Company's Chief Financial Officer from November 5, 2009 through December 2013, and has been President since November 2010. On January 1, 2014, Thero was promoted to the position of CEO and director on Amarin's Board of Directors. During the Class Period and before Amarin's ADS's declined on November 12-13, 2018, Thero sold 622,368 shares for profits of approximately $11.27 million.

16. Defendant Steven Ketchum, PhD was, at all relevant times, President of Research and Development, Senior Vice President, and CSO of the Company. During the Class Period, Ketchum sold 1,212,887 Amarin shares for insider trading profits of $8,368,474.65.

17. Defendant Craig B. Granowitz, MD, PhD, was appointed as Amarin's Senior Vice President and Chief Medical Officer ("**CMO**") in January 2016.

18. Defendant Joseph S. Zakrzewski was at all relevant times a member of the Company's Board of Directors. Zakrzewski was CEO of the Company, and Chairman of its Board of Directors from November 2010 to December 2013. During the Class Period, Zakrzewski sold 500,000 Amarin shares for insider trading profits of $3.6 million.

19. Defendants Thero, Ketchum, and Granowitz are collectively referred to herein as the "Officer Defendants," and together with the addition of Zakrzewski are collectively referred to as the "Individual Defendants."

20. During the Class Period, the Individual Defendants, as senior executive officers and directors of Amarin, were privy to confidential and proprietary information concerning Amarin, its operations, product, finances, financial condition, and present and future business prospects. The Individual Defendants also had access to material adverse non-public information concerning Amarin, its singular product, Vascepa, and its flagship REDUCE-IT trial, as detailed below. The Individual Defendants had access to non-public information about Amarin's business, products, finances, markets and present and future business prospects via access to internal corporate documents, conversations and connections with other corporate officers and employees, attendance at management and board of directors meetings and committees thereof, and via reports and other information provided to them in connection therewith. Because of their possession of such information, the Officer Defendants knew or recklessly disregarded that the adverse facts contradicting their misrepresentations and relating to their omissions had not been disclosed to, and were being concealed from, the investing public.

21. The Individual Defendants are liable as direct participants in, and as co-conspirators with respect to, the wrongs complained of herein. In addition, the Individual Defendants, by reason of their status as senior executive officers and directors were "controlling persons" within the meaning of §20(a) of the Exchange Act and had the power and influence to cause the Company to engage in the unlawful conduct complained of herein. Because of their positions of control, the Individual Defendants were able to and did control the conduct of Amarin's business.

22. The Individual Defendants, because of their positions with the Company, controlled or possessed the authority to control the contents of its reports, press releases, and presentations to securities analysts and through them, to the investing public. Thus, the Individual Defendants were authorized agents of the Company, having permission and authority to speak on behalf of Amarin. The Individual Defendants were provided with copies of the Company's statements alleged herein to be misleading, prior to or shortly after their issuance and had the ability and opportunity to prevent their issuance or cause them to be corrected. Thus, the Individual Defendants had the opportunity to commit the fraudulent acts alleged herein.

23. As senior executive officers and directors and as controlling persons of a publicly traded company whose ADS's were and are registered with the SEC pursuant to the Exchange Act, and were traded on the NASDAQ Global Market, and governed by the federal securities laws, the Individual Defendants had a duty to promptly disseminate accurate and truthful information about Amarin's financial condition and performance, growth operations, financial statements, business, product, markets, management, earnings, and present and future business prospects, to correct any previously issued statements that were or had become materially misleading or untrue, so that the market price of Amarin's shares would be based upon truthful

and accurate information. The Officer Defendants' misrepresentations and omissions during the Class Period violated these specific requirements and obligations.

24. The Officer Defendants are liable as participants in a course of conduct that operated as a fraud on the purchasers of Amarin's publicly traded ADS's by disseminating materially false and misleading statements and concealing material adverse facts. The scheme: (i) deceived the investing public regarding Amarin's business, product, operations, management, and the intrinsic value of Amarin's shares; (ii) enabled Defendants Thero, Ketchum, and Zakrzewski, as well as non-party executives Joseph T. Kennedy and Michael Wayne Kalb, to sell over 3.47 million of their personally held Amarin shares at artificially inflated prices and thereby reap over $34.9 million in profits; and (iii) caused Plaintiffs and members of the Class to purchase Amarin shares at artificially inflated prices.

IV. FACTUAL BACKGROUND

A. Cardiovascular Disease

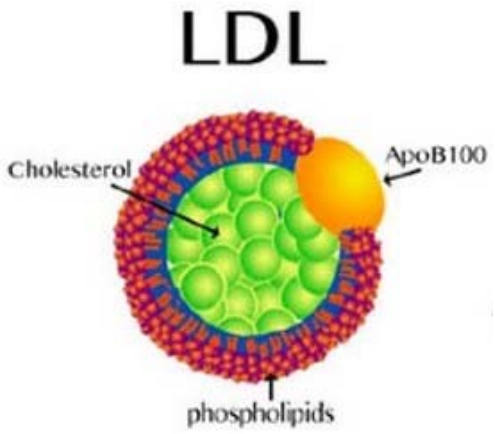
25. Atherosclerotic cardiovascular disease (*i.e.*, plaque buildup in the arteries) and its clinical manifestations, such as myocardial infarction (a/k/a heart attack) and ischemic stroke, are the leading cause of morbidity and mortality throughout the world. Brian A. Ference, et al., *Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies*, 38 Euro. Heart J. 2459 (2017).

26. Atherosclerotic cardiovascular disease is caused, in part, by excessive levels of certain lipids and lipoproteins in the blood. *See id.* Two types of lipids (*i.e.*, fat-like substances) found in the blood are cholesterol and triglycerides. *Triglycerides: Why Do They Matter?*, Mayo Clinic (Sept. 13, 2018), https://www.mayoclinic.org/diseases-conditions/high-blood-cholesterol/in-depth/triglycerides/art-20048186. Because these two lipids are insoluble in water, they must join up with proteins, forming lipoproteins, in order to be transported through the

blood. Kenneth R Feingold, MD & Carl Grunfeld, MD, PhD, *Introduction to Lipids and Lipoproteins*, Endotext.com (2018).

27. There are seven classes of lipoproteins, one of the most important being low-density lipoproteins ("**LDL**"). *See id.* LDLs carry the majority of the cholesterol that is in circulation in the blood, known as "**LDL-Cholesterol**" or "**LDL-C**."[1] *See id.*

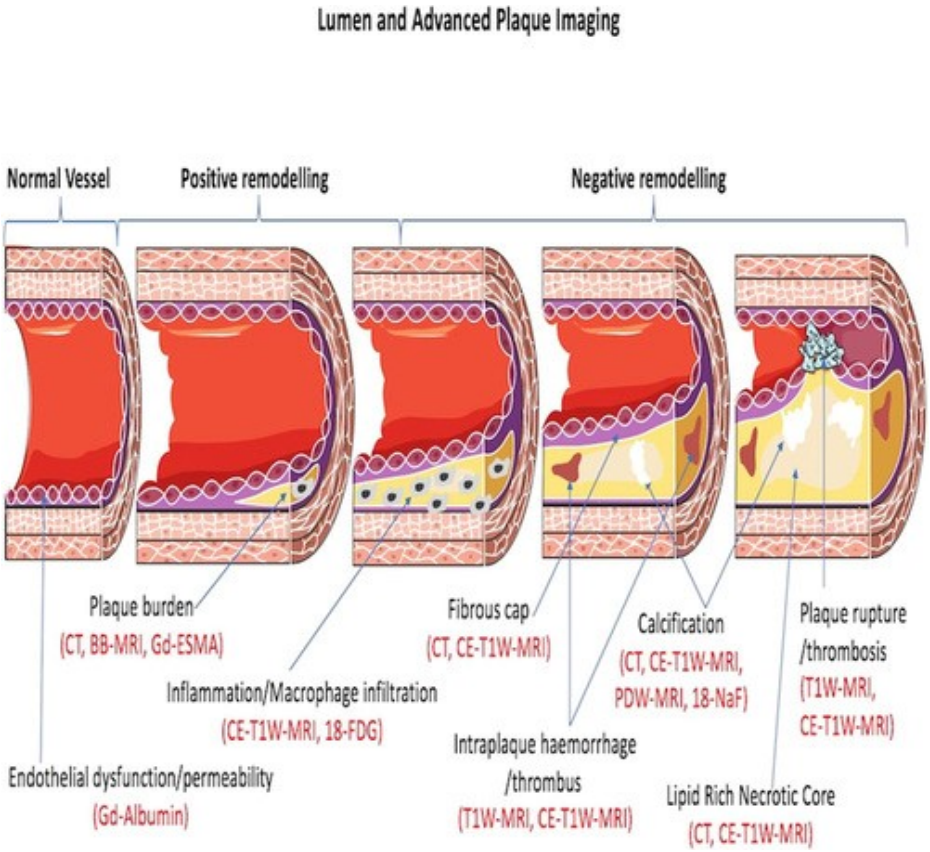
28. Apolipoproteins are proteins that bind lipids to form lipoproteins. The Free Dictionary, Medical Dictionary, https://medical-dictionary.thefreedictionary.com/apolipoprotein (last visited July 21, 2019). Apolipoproteins are thus crucial to the formation and metabolism of lipoproteins in the blood. Kenneth R Feingold, MD & Carl Grunfeld, MD, PhD, *Introduction to Lipids and Lipoproteins*, Endotext.com (2018). Each LDL particle contains one apolipoprotein B-100 molecule ("**Apo B**"). *See id.* Below is a computer-generated image of LDL-C:



See Aridaya and Alan's Cholesterol Fun, https://cholesterolfun.weebly.com/ldl--hdl-tab.html (last visited June 26, 2019).

[1] High-density lipoprotein ("**HDL**") is another important lipoprotein which carries cholesterol known as HDL-Cholesterol or "**HDL-C**" away from the peripheral tissues in the body and delivers it to the liver, thereby "disposing of" the cholesterol in the body. *See id.*

29. Atherosclerosis is the process of plaque buildup or "calcification" of the arteries. If LDL-C particles in the blood are increased, usually as a result of a high fat diet, diabetes, or genetic factors, when they leave the blood and enter into the lining of the artery, they begin to accumulate in the lining. *See* William Insull Jr., *MD, The Pathology of Atherosclerosis: Plaque Development and Plaque Responses to Medical Treatment*, 122 Am. J. of Med. S3 (2009). As the LDL-C particles accumulate in the lining of the artery, they activate an inflammatory reaction whereby white blood cells begin to attach to the lining. *See id.* When the white blood cells enter into the lining of the artery, they transform into foam cells and attract lipids to form fatty deposits. *See id.* This increasing inflammation and accumulation of lipids is referred to as the "plaque" buildup in the arteries. *See id.* Calcium deposits also develop in the inflamed wall of the arteries which leads to a hardening of the tissue. *See id.* Below is an image depicting the buildup of plaque in the arteries:



See Reza Hajhosseiny, et al., *Molecular and Nonmolecular Magnetic Resonance Coronary and Carotid Imaging*, 39 Arterioscler. Thromb. Vasc. Biol. 569 (2019).

30. As a person ages and plaque buildup continues, the arterial wall may become so enlarged that blood flow becomes sufficiently restricted to cause a heart attack or stroke. *See* William Insull Jr., *MD, The Pathology of Atherosclerosis: Plaque Development and Plaque Responses to Medical Treatment*, 122 Am. J. of Med. S3 (2009). In other cases, the arterial wall may become thinned and weakened, causing a rupture. *See id.* Such ruptures result in the formation of a blood clot in the artery which restricts blood flow and may result in a heart attack or stroke. *See id.*

31. Through a series of tests in the 1970's, researchers discovered several chemicals, known as "statins," which inhibit the primary enzyme responsible for synthesizing cholesterol, HMG-CoA reductase. *See* David Pineles, MD, *On The History of Statins*, Clinical Correlations (Jan. 11, 2019), https://www.clinicalcorrelations.org/2019/01/11/on-the-history-of-statins/. Human trials of these statins showed that inhibition of HMG-CoA reductase activates the LDL receptors in the liver,[2] thereby lowering the concentration of LDL-C in the blood. *See id.* In the years that followed, pharmaceutical companies took note and began developing statins as a potential treatment for atherosclerotic cardiovascular disease. *See id.* Today, statin therapy, including, Lipitor® (atorvastatin), Lescol® (fluvastatin), Mevacor® (lovastatin), Altoprev® (lovastatin extended-release), Livalo® (pitavastatin), Pravachol® (pravastatin), Crestor®

[2] Two important functions of the liver are to filter and detoxify blood and absorb fat in the body. *See* Tim Newman, *What does the liver do?*, Medical News Today (Mar. 2, 2018), https://www.medicalnewstoday.com/articles/305075.php.

(rosuvastatin), and Zocor® (simvastatin), are the first-line standard-of-care[3] for treating atherosclerotic cardiovascular disease by lowering LDL-C levels. *See Statins*, U.S. Food & Drug Administration (Dec. 16, 2014) https://www.fda.gov/drugs/information-drug-class/statins; *see also* Mary Dunne Roberts, MD, U.S. Food & Drug Admin., *Clinical Review: Endocrinologic and Metabolic Advisory Committee Meeting October 16, 2013* 10 (2013) ("**FDA Briefing Document**" or "**FDA Br. Doc.**") (prepared in connection with Amarin's application for the ANCHOR indication, *see* ¶49).

32. While statins are currently the standard of care for lowering LDL-C levels, many patients retain a high cardiovascular risk despite achieving their recommended LDL-C targets while taking statins. Based on a series of large statin trials, optimal statin treatment reduces cardiovascular events by 30-40% over five years, meaning that many patients treated to their LDL-C goal still have residual risks. *See* Amarin Pharms. Ireland, Ltd., *Briefing Document for the Endocrinologic and Metabolic Drugs Advisory Committee Meeting* 9 (2013) ("**Amarin Briefing Document**" or "**Amarin Br. Doc.**") (prepared in connection with Amarin's application for the ANCHOR indication, *see* ¶52).

B. Vascepa®

33. Amarin has been developing Icosapent ethyl, a/k/a Vascepa®, to address the remaining 60-70% risk of cardiovascular events which are not addressed by statin treatment. *See id.* at 23-24. Vascepa is made up of a single omega-3 fatty acid: eicosapentaenoic acid ("**EPA**") derived from fish oil. FDA Br. Doc. at 1. According to Amarin, EPA has been associated with

[3] First-line standard-of-care therapy is a term used to describe the therapy that is considered the best treatment for a disease or condition. *See* NCI Dictionary of Cancer Terms, National Cancer Institute, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/first-line-therapy (last visited July 15, 2019).

cardiovascular benefits including reducing triglyceride levels, inhibiting platelet aggregation, stabilizing plaque, causing anti-inflammatory effects, and improving blood flow. *See id.*

34. Amarin has tested Vascepa's ability to treat two specific types of lipid disorders called hypertriglyceridemia and mixed dyslipidemia. *See id.* at 3. Hypertriglyceridemia is a condition diagnosed when blood triglyceride levels rise above a threshold value, such as the 90th or 95th percentile depending upon factors such as age and gender. *See* Amanda Brahm & Robert A. Hegele, *Hypertriglyceridemia*, 5 Nutrients 981 (2013). The two categories of hypertriglyceridemia are moderate hypertriglyceridemia (blood triglyceride levels between 175-499 mg/dL of blood plasma) and severe hypertriglyceridemia (blood triglyceride levels ≥ 500 mg/dL of blood plasma). *See* Scott M. Grundy MD, PhD, FAHA, et al., *A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines*, 73 J. of Am. Coll. of Cardiology 285 (2018). Hypertriglyceridemia typically results from a combination of genetic factors and other causes of overproduction or impaired clearance of triglycerides, such as obesity, physical inactivity, excessive alcohol intake, metabolic syndrome, type 2 diabetes mellitus, and certain medications. *See* Lars Berglund et al., *Evaluation and Treatment of Hypertriglyceridemia: An Endocrine Society Clinical Practice Guideline*, 97 J. of Clinical Endocrinology & Metabolism 2969 (2012). Severe and moderate hypertriglyceridemia increases a person's risk for cardiovascular disease. *Id.* It is estimated that more than 10 million people in the United States have been diagnosed with hypertriglyceridemia. Amarin Corp. plc, Report of Foreign Private Issuer (Form 6-K) (July 22, 2008).

35. Mixed dyslipidemia is defined as the presence of abnormally high LDL-C levels combined with at least one other lipid abnormality, such as high triglyceride levels. FDA Br. Doc. at 6. The primary causes of mixed dyslipidemia are gene mutations which result in either

overproduction or defective clearance of triglycerides and LDL-C from the blood, or an underproduction or excessive clearance of HDL-C. Anne Carol Goldberg, *Dyslipidemia*, Merck Manuals Professional Version (Mar. 2018), https://www.merckmanuals.com/professional/endocrine-and-metabolic-disorders/lipid-disorders/dyslipidemia. The secondary causes of mixed dyslipidemia are excessive alcohol or fat intake, type 2 diabetes mellitus, chronic kidney disease, hypothyroidism, liver diseases, and certain medications. *See id.* If left untreated, mixed dyslipidemia can lead to cardiovascular disease. *See id.*

C. Amarin Begins Three Phase 3 Trials of Vascepa

36. In July 2008, Amarin senior officers met with the FDA for the purpose of discussing the Company's plans to develop Vascepa[4] for the treatment of hypertriglyceridemia and mixed dyslipidemia. Amarin Corp. plc, Report of Foreign Private Issuer (Form 6-K) (July 22, 2008). The Company and the FDA agreed upon a Phase 3[5] trial program with three pivotal trials to test the drug in patients with these disorders. *See id.*

1. The MARINE Trial

37. Patient enrollment for the first Phase 3 trial, the MARINE trial, began in December 2009. *See* Amarin Corp. plc, Annual Report (Form 10-K) at 7 (Feb. 29, 2012). The

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[4] The drug was then known as "AMR 101" but is referred to herein as Vascepa for consistency's sake.

[5] Clinical testing of a drug is broken down into four phases based upon the size and purpose of the trials. The Phase 3 trial stage involves randomized and blind testing in several hundred to several thousand patients. Overview of Clinical Trials, Center Watch, https://www.centerwatch.com/clinical-trials/overview.aspx/ (last visited July 15, 2018). This large-scale testing, which can last several years, provides the pharmaceutical company and the FDA with a more thorough understanding of the effectiveness of the drug and the range of possible adverse reactions. *Id.* Once Phase 3 is complete, a pharmaceutical company can request FDA approval for marketing the drug. *Id.*

MARINE trial was a placebo-controlled, randomized, double-blind, 12-week study designed to test Vascepa in patients who have severe hypertriglyceridemia, with triglyceride levels ≥ 500 mg/dL. *See* Amarin Corp. plc, Annual Report (Form 10-K) at 7 (Feb. 29, 2012). Patients were randomized into three treatment arms for treatment with Vascepa at 4 grams/day, Vascepa at 2 grams/day, or placebo. *See id.* The primary endpoint[6] of the MARINE trial was the percentage change in triglyceride levels from baseline[7] compared to placebo after 12 weeks of treatment. *See id.* Both Vascepa and the placebo were packaged into capsules, with the placebo capsules being filled with mineral oil, also known as liquid paraffin, ostensibly because the oil looks similar to EPA. *See* Amarin Br. Doc. at 15.

38. At the time, Amarin estimated that in the United States approximately 4 million people had been diagnosed with severe hypertriglyceridemia. *See* Amarin Corp. plc, Current Report (Form 8-K) (July 27, 2012).

39. On November 29, 2010, Amarin announced that the MARINE trial had met its primary endpoint with median reductions in triglyceride levels of 33% compared to placebo for 4 grams of Vascepa per day and 20% compared to placebo for 2 grams of Vascepa per day. Amarin Corp. plc, Report of Foreign Private Issuer (Form 6-K) (November 29, 2010).

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[6] A "primary endpoint" is the main, pre-determined measure of the trial to establish the effectiveness and/or safety features of a drug in order to support approval by the FDA. A "secondary endpoint" is a measure selected to demonstrate additional effects or benefits of a drug. *See* Peter R. Nelson, *Primary and Secondary Endpoints*, *in* Clinical Trials Design in Operative and Non Operative Invasive Procedures 11 (Kamal M.F. Itani & Domenic J. Reda eds., 2017).

[7] In clinical trials, "baseline" means the measurement of a condition in a patient before treatment is administered. *See NCI Dictionary of Cancer Terms*, National Cancer Institute, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/baseline (last visited July 8, 2019).

40. In September 2011, Amarin submitted a New Drug Application ("**NDA**") to the FDA requesting approval to market and sell Vascepa for the indication[8] studied in the MARINE trial, *i.e.* treatment with Vascepa to reducte triglyceride levels for patients with severe hypertriglyceridemia (triglycerides ≥ 500 mg/dL). Amarin Corp. plc, Current Report (Form 8-K) (November 8, 2011). The NDA included supportive safety and efficacy data gathered from the MARINE trial as well as the subsequent ANCHOR trial (discussed below). *Id.*

41. On July 26, 2012, Amarin announced that the FDA had approved Vascepa capsules as an adjunct to diet to reduce triglyceride levels in adult patients with severe hypertriglyceridemia (triglycerides ≥ 500 mg/dL) based on the positive MARINE trial results. Amarin Corp. plc, Current Report (Form 8-K) (July 27, 2012). Thereafter, in January 2013, Amarin began selling and marketing Vascepa by prescription only based on the FDA-approved MARINE indication for patients with severe hypertriglyceridemia (triglycerides ≥ 500 mg/dL). Amarin Corp. plc, Quarterly Report (Form 10-Q) at 24 (May 1, 2019).

2. The ANCHOR Trial

42. Amarin initiated its second pivotal Phase 3 clinical trial of Vascepa, the ANCHOR trial, in January 2010. Amarin Corp. plc, Annual Report (Form 10-K) at 9 (Feb. 27, 2014). The purpose of the ANCHOR trial was to test Vascepa's effectiveness in reducing triglycerides without raising LDL-C levels in a population with high, but not very high triglycerides, who were already taking statins. *See* Press Release, Amarin Corp. plc, Amarin's AMR101 Phase 3 ANCHOR Trial Meets all Primary and Secondary Endpoints with Statistically Significant Reductions in Triglycerides at Both 4 Gram and 2 Gram Doses and Statistically

[8] In medical terminology, an "indication" for a drug refers to the use of that drug to treat a particular disease or condition. Jay Marks, M.D., *Indications for Drugs (uses), Approved vs. Non-approved*, MedicineNet (June 13, 2018), https://www.medicinenet.com/indications_for_drugs__approved_vs_non-approved/views.htm.

Significant Decrease in LDL-C (Apr. 18, 2011). The ANCHOR trial was a placebo-controlled, randomized, double-blind, 12-week trial in patients who have mixed dyslipidemia and, despite being on statin treatment to achieve controlled LDL-C levels between ≥ 40 mg/dL and ≤ 115 mg/dL, still have high triglyceride levels between 185 and < 500 mg/dL. Amarin Br. Doc. at 13. 702 patients enrolled in the trial and they were randomized into three arms for treatment with Vascepa at 4 grams/day, Vascepa at 2 grams/day, or placebo. *See id.* All patients took statins during the ANCHOR trial, and the placebo used was the same mineral oil used in the MARINE trial. Amarin Br. Doc. at 14-15. The primary endpoint of the trial was the percentage change in triglyceride levels from baseline compared to placebo after 12 weeks of treatment. Amarin Corp. plc, Annual Report (Form 10-K) at 9 (Feb. 27, 2014).

43. On April 18, 2011, Amarin reported top-line results from the ANCHOR trial. Amarin Corp. plc, Current Report (Form 8-K) (Apr. 18, 2011). The ANCHOR trial met its primary endpoint with statistically significant results. *See id.* Specifically, the results showed median reductions in triglyceride levels of 21.5% compared to placebo for 4 grams of Vascepa per day and 10.1% compared to placebo for 2 grams of Vascepa per day. *See id.*

3. The REDUCE-IT Trial

44. Several months later, on November 28, 2011, Amarin initiated its third and largest Phase 3 trial of Vascepa, the REDUCE-IT trial. *See* Deepak L. Bhatt, M.D., M.P.H., et al., *Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia*, 380 N. Engl. J. Med. 11, 12 (2018) ("**NEJM Article**"). The purpose of the trial was to evaluate whether Vascepa, combined with statin therapy, is superior to statin therapy alone, when used as a prevention in reducing long-term cardiovascular events in high-risk patients with mixed dyslipidemia. *Id.* The REDUCE-IT trial was a randomized, double-blind, placebo-controlled trial that enrolled patients who had mixed dyslipidemia, with LDL-C levels controlled to

between 41-100 mg/dL by statin therapy and high triglyceride levels between 150-499 mg/dL, along with either established cardiovascular disease or diabetes mellitus and at least one other cardiovascular risk factor. *Id.* 8,179 patients were enrolled in the trial, and they were randomized into two arms for treatment with one arm receiving Vascepa at 4 grams/day and the other arm receiving the placebo. *Id.* The trial used the same mineral oil placebo that was used in the MARINE and ANCHOR trials. *See* Amarin Br. Doc. at 15.

45. Patients were followed in the REDUCE-IT trial for a median of four years. NEJM Article at 13. Unlike the MARINE and ANCHOR trials where the primary endpoint was the reduction in triglycerides, the primary efficacy endpoint of the REDUCE-IT trial was a composite of the first occurrence of a "Major Adverse Cardiac Event" or "**MACE**," including cardiovascular death, nonfatal myocardial infarction (a/k/a nonfatal heart attack), nonfatal stroke, coronary revascularization (*i.e.*, heart surgery such as stent placement or bypass surgery), or unstable angina (*i.e.*, poor blood flow through the arteries due to blood clots). NEJM Article at 13. The endpoint was measured in a time-to-event analysis, meaning that the trial studied the time it took for a patient to experience a primary endpoint MACE event. *Id.* The trial also included several secondary endpoints, including a key secondary endpoint which was a composite of the first occurrence of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke in a time-to-event analysis. *Id.* Due to the size and the length of the REDUCE-IT trial, Amarin established an independent data monitoring committee to conduct safety and interim analyses. *See* Amarin Corp. plc, Clinical Study Protocol, Amendment #1, 44 (May 16, 2013).

46. The proposed indication for the REDUCE-IT trial was treatment with Vascepa as an add-on to statin therapy to reduce the risk of cardiovascular events in patients with clinical

cardiovascular disease or with multiple risk factors for cardiovascular disease. Amarin Corp. plc, Clinical Study Protocol, Amendment #2, 3 (July 8, 2016). In contrast to the potential patient population of the MARINE indication of 4 million people (¶38), when the REDUCE-IT trial was initiated, Amarin estimated that the indication could address a patient population of more than 70 million in the United States alone. Press Release, Amarin Corp., plc, Amarin Commences 2012 with Letter to Shareholders (Jan. 3, 2012).

D. The FDA Rejects Expanded Approval of Vascepa Based on the ANCHOR Trial

47. While the ANCHOR trial had met its primary endpoint, comparisons between the treatment arms and the placebo arm for several lipid and lipoprotein biomarkers[9] indicated that the placebo arm was performing abnormally for patients on cholesterol-lowering statins because key biomarker levels were ***increasing*** in the placebo arm instead of remaining relatively constant from baseline. *See* FDA Br. Doc. at 53. For example, a comparison of the LDL-C levels between the three arms shows that patients in the Vascepa 4 grams/day arm experienced a 1.5% increase in LDL-C from baseline, and patients in the Vascepa 2 grams/day arm experienced a 2.4% increase from baseline; however, patients in the placebo arm experienced a significantly larger ***8.8% increase*** in LDL-C from baseline. Amarin Br. Doc. at 21. Similarly, for Apo B, patients in the Vascepa 4 grams/day arm experienced a 2.2% decrease in Apo B from baseline, and patients in the Vascepa 2 grams/day arm experienced a 1.6% increase from baseline, whereas, patients in the placebo arm experienced a much higher ***7.1% increase*** in Apo B from baseline. *See id.* A comparison of the non-HDL-C (meaning all of the cholesterol contained in

[9] A "biomarker" "refers to a broad subcategory of medical signs—that is, objective indications of medical state observed from outside the patient—which can be measured accurately and reproducibly." Kyle Strimbu and Jorge A. Tavel, M.D., *What are Biomarkers?*, 5 Curr Opin HIV AIDS 463 (2011).

lipoproteins that is not HDL-C), showed that patients in the Vascepa 4 grams/day arm experienced a 5.0% decrease in non-HDL-C from baseline, and patients in the Vascepa 2 grams/day arm experienced a 2.4% increase from baseline, whereas patients in the placebo arm experienced a notable ***9.8% increase*** in non-HDL-C from baseline. *See id.*

48. Because all of the patients in the trial were supposed to be taking statins along with either Vascepa or placebo, the statins *should* have kept the LDL-C, non-HDL-C, and Apo B levels consistent with the patients' entry baseline numbers because statin therapy is designed to control cholesterol levels. *See* David Pineles, MD., *On The History of Statins*, Clinical Correlations (Jan. 11, 2019), https://www.clinicalcorrelations.org/2019/01/11/on-the-history-of-statins/. Thus, the sizeable increases in the LDL-C, non-HDL-C, and Apo B values observed in the placebo arm indicated that the statins were not performing as expected in those patients. Because the purpose of the trial was to compare the effect of Vascepa to statin therapy alone, if the statin therapy in the placebo arm was not operating properly, the treatment effect in the Vascepa arm would have been overstated.

49. Despite the red flags in the placebo arm of the ANCHOR trial, on February 21, 2013, Amarin filed an supplemental new drug application ("**sNDA**") with the FDA seeking expanded approval of Vascepa based upon the ANCHOR indication, *i.e.*, Vascepa treatment as an adjunct to diet and exercise and in combination with a statin to reduce triglyceride, non-HDL-C, Apo B, LDL-C, TC, and VLDL-C in adult patients with mixed dyslipidemia and coronary heart disease or a coronary heart disease equivalent. FDA Br. Doc. at 6, 12. As part of its review process, the FDA scheduled a meeting of the Endocrinologic and Metabolic Drugs Advisory Committee ("**Advisory Committee**") to be held on October 16, 2013 (the "**Advisory Committee Meeting**"). FDA Br. Doc. at 1. Advisory committees provide the FDA with

independent advice from outside experts on drug applications, although the final approval decision is left up to the FDA. *What Is An Advisory Committee?*, U.S. Food & Drug Administration (Mar. 28, 2018), https://www.fda.gov/about-fda/fda-basics/what-fda-advisory-committee. Prior to the Advisory Committee Meeting, on October 11, 2013, the FDA published a briefing document (defined in ¶31 *supra* as the FDA Briefing Document) to provide assessments, recommendations, and conclusions regarding the sNDA for Amarin and the panel members of the advisory committee. *See* FDA Br. Doc.

50. In the FDA Briefing Document, the FDA raised two important problems with the ANCHOR trial data. First, the FDA explained that in 2008 it had told Amarin that there was insufficient data at the time to support the hypothesis that lowering triglyceride levels reduces cardiovascular risk. FDA Br. Doc. at 9. The FDA explained in the Briefing Document that because two other triglyceride-lowering trials conducted by other companies have subsequently failed, it challenges the hypothesis that adding triglyceride-lowering therapies to statins will reduce cardiovascular risk. *Id.*

51. Second, in the FDA Briefing Document, the FDA explained its concerns that the placebo data in the ANCHOR trial indicated that the mineral oil placebo may not have been inert (*i.e.*, chemically inactive), and thus may have biased the treatment effect of Vascepa, stating:

- "Although it is recognized that the effect of an intervention (e.g., mineral oil capsules) cannot be isolated when one only considers within-group changes over time, ***these results at least suggest the possibility that mineral oil may not be biologically inert***. ***If true, this complicates the interpretation of between-group differences***."

- "Also, note that for each of these parameters, with the exception of HDL-C and apo A1, the placebo group demonstrated nominally statistically significant changes from baseline in an adverse direction, while on background statin therapy. If these within-group changes were the result of factors that were randomly distributed across treatment groups, the comparisons to placebo should represent the best estimates of the

> treatment effect. ***If it is possible, however, that the mineral oil placebo was not biologically inert (e.g., could it have partially inhibited statin absorption if concomitantly ingested?), then the comparisons with placebo could produce biased treatment effects***. This possibility that the placebo may not be inert is further discussed in Section 5.5."
>
> - "[T]he magnitude of the changes in several lipid and lipoprotein parameters, as well as biomarkers of inflammation, between baseline and Week 12 in the placebo group are rather atypical for lipid-lowering trials. These trials, including ANCHOR, often include a several-week lead-in period to stabilize diet and concomitant lipid-altering medications well before baseline measurements. Although even highly statistically significant within-group changes can certainly result from factors other than the intended experimental intervention, ***one concerning possibility is that the mineral oil placebo may not be biologically inert. If this were true, the estimated treatment effects may be biased***."

Id. at 7, 40, 53-55.

52. Amarin also prepared a briefing document (defined above as the "Amarin Briefing Document") that it provided to the advisory committee panel. *See* Amarin Br. Doc. In the Amarin Briefing Document, the Company attempted to explain away the issues with the placebo arm noted by the FDA, stating, in part:

> Although isolated earlier publications suggested that mineral oil may interfere with the absorption of fat-soluble substances, more recent reports (Sharif 2001, and Gal-Ezar 2006) concluded that mineral oil induced fat-soluble vitamin deficiency is unfounded, indicating that this is not expected at the low doses used in ANCHOR. Overall, LLP was chosen as placebo because it is chemically inert, has minimal absorption, does not alter lipids, is well matched with Vascepa for color, is safe, and does not interfere with the absorption of fat soluble vitamins at the doses used in the ANCHOR study. ***There is no scientific evidence that trends for increase in lipid parameters in the placebo arm in the at-risk patient population that was studied in ANCHOR were caused by the placebo and, as described herein, Vascepa's overall results were favourable both on a placebo corrected and non-placebo corrected basis***.

Id. at 15.

53. After the FDA published its Briefing Document on October 11, 2013, which included the revelations that reductions in triglyceride levels may not be sufficient to support approval of the ANCHOR indication and that the mineral oil in the placebo arm may have

caused a biased treatment effect, Amarin's ADS's suffered a substantial decline in value. On October 11, 2013, Amarin's shares declined by $1.28 per share—from $6.37 to $5.09, an over 20% decline—on volume of over 37.9 million shares. Amarin Corporation plc, Historical Data, Yahoo!Finance, https://finance.yahoo.com/quote/AMRN/history?period1=1380600000&period2=1383278400&interval=1d&filter=history&frequency=1d (last visited July 7, 2019).

54. During the Advisory Committee Meeting held on October 16, 2013, several committee members again remarked that the most contemporary evidence has not supported the hypothesis that lowering triglycerides with a drug leads to cardiovascular benefit. *Id.* Food and Drug Administration, Center for Drug Evaluation and Research, Summary Minutes of the Endocrinologic and Metabolic Drugs Advisory Committee Meeting, 5 (Oct. 16, 2013).

55. Several others, including the FDA's Clinical Reviewer, Mary Dunne Roberts, MD also reiterated the FDA's concern that the lipid and lipoprotein biomarker data observed in the placebo arm of the ANCHOR trial indicated that mineral oil placebo may not be inert. Dr. Roberts also raised the possibility that the mineral oil placebo may cause problems in the REDUCE-IT trial; and thus, the FDA spoke with Amarin about the issue and requested that the Company task the REDUCE-IT data monitoring committee to keep these concerns in mind when monitoring the lipid data:

> In the case of ANCHOR, however, ***the changes observed within the placebo group stood out as atypical for similarly designed lipid-lowering trials that we have reviewed, which gave us pause***, ***especially since the changes went in an unfavorable direction***. Thus, the review team sought evidence that might help explain the changes observed in the mineral oil group. We considered issues with randomization, unblinding, statin absorption, study design elements, and lipid changes in placebo-treated patients. Our review did not point to any particular cause for the observed placebo changes. Therefore, what if any implications do the placebo group changes have on the REDUCE-IT and ANCHOR trials? ***For REDUCE-IT, our primary concern was whether or not there was a possibility that the mineral oil could attenuate the effect of a statin, perhaps by inhibiting absorption. If plausible, this would raise concerns about the potential impact***

> ***this would have on the ongoing cardiovascular outcomes trial, which is also using mineral oil as placebo among statin-treated patients***. Because we do not have any hard evidence for an interaction, such as a formal drug-drug interaction study, ***we discussed our concern with the sponsor and asked that they task the REDUCE-IT data monitoring committee with evaluating the accruing lipid data with this concern in mind***.
>
> What implications are there, if any, for the ANCHOR trial? There could be none. If one believes that all elements affecting outcomes in the ANCHOR trial were equally distributed between the placebo and active groups, then the between-group comparisons represent the best estimate of the treatment effect, shown in the far right column of this table. Alternatively, ***if one believes that the changes within the placebo group could be a result of some factor that is not also present in the active groups, then the treatment effect of Vascepa may be overestimated. This may or may not affect your interpretation of whether these results would be expected to translate into a benefit on clinical outcomes***. These possible implications may be kept in mind when considering the following summary statements regarding efficacy in the ANCHOR trial.

Transcript of Endocrinologic and Metabolic Drugs Advisory Committee Meeting, 139-141 (Oct. 16, 2013), *available at* http://epadruginitiative.com/files/Vascepa_ADCOM_Transcript.docx.

56. Panel members also voiced their concerns that the mineral oil placebo used in the ANCHOR trial may not be inert. One member even suggested that the FDA look to the REDUCE-IT trial's results to confirm whether mineral oil is an inert placebo, stating in part:

- Robert J. Smith, MD: "A key point that ***I still feel very uncomfortable about the proper control group***. Have heard all the arguments, and I've thought about them here and before coming here. ***But I remain uncomfortable with comparisons against the placebo*** . . . But the point is that I feel, ***in trying to address this question of the observed changes in these lipid and lipoprotein parameters, I feel uncomfortable with what a number of those changes are***. . . . So again, ***I'm just reemphasizing my concern about whether the data derived against the placebo control we have are overstating the degree of change in some of these lipid endpoints***. . . ."

- William R. Hiatt, MD, FACP: "The placebo responses were interesting, and I appreciate the FDA and the sponsor's attempt to explain it, which they couldn't. It's a small study. I mean, ***it's possible that it's a fluke, and it may not play out in the REDUCE-IT trial. I think that that trial***

> ***will perhaps inform whether that's a biologically accurate placebo or inert placebo***. Even if you subtract that out, the changes from baseline are pretty dramatic on triglyceride as the primary, so I don't think the drug is inert. It's biologically active. It's changing the primary endpoint significantly. ***You could ask the DMC of REDUCE-IT to monitor the placebo changes, perhaps, and ask if they see signals of concern***. I'm not sure what you'd do about it. But it may not reappear."

Id. at 270-73.

57. In contrast, the Company's presentation during the Advisory Committee Meeting, provided in part by Ketchum, recognized the "possibility of some type of inhibition of statin absorption" but attempted to minimize the issues and deny that the mineral oil interfered with the statins. Ketchum provided three explanations for the biomarkers in the placebo arm, as set forth in his own words below:

> But turning to your question about the mineral oil, I'd like to share with you our systemic evaluation of mineral oil. . . . As I go through this, I'd like to share with you some historical precedents, both in our studies with mineral oil but in others who've used a mineral oil placebo. And then I'd like to put it in a mixed dyslipidemia context in terms of range of trials and similar type of duration as ANCHOR with a variety of oil and non-oil placebos. I'd like to speak to the possibility of some type of inhibition of statin absorption. It's obviously important in this context of an add-on therapy a statin. And also, the possibility of some type of underlying drift of lipid values in the placebo patients. . . .

Id. at 104-108.

58. Despite his statements acknowledging potential issues with the mineral oil placebo, however, Ketchum's conclusion was: "that we do not fully understand what contributed to this drift." *Id.* at 108.

59. Nine of the eleven committee members ultimately voted "NO" to approval of the sNDA based upon the ANCHOR indication, stating that although the triglyceride-lowering effect was clear, the clinical benefit of overall cardiovascular risk reduction remained uncertain. Food

and Drug Administration, Center for Drug Evaluation and Research, Summary Minutes of the Endocrinologic and Metabolic Drugs Advisory Committee Meeting, 5 (Oct. 16, 2013).

60. The FDA's concern that the mineral oil placebo used in the ANCHOR trial may have affected absorption of patients' statins is not novel. It has been widely reported that because mineral oil acts a laxative, prolonged use can interfere with absorption of vitamins and minerals. *See Mineral Oil*, National Multiple Sclerosis Society, https://www.nationalmssociety .org/Treating-MS/Medications/Mineral-oil (last visited June 27, 2019); Sharon Gal-Ezer, MD & Ron Shaoul, MD, *The Safety of Mineral Oil in the Treatment of Constipation—A Lesson from Prolonged Overdose*, 45 Clin. Pediatr. 856 (2006); George L. Becker, *The Case Against Mineral Oil*, 19 Am. J. of Digestive Diseases 344 (1952). Indeed, the problem is so prevalent that FDA regulations contain a section entitled "Notice to manufacturers, packers, and distributors of drugs for internal use which contain mineral oil" (promulgated in 1975) warning manufacturers that research studies "have indicated that when mineral oil is used orally near mealtime it interferes with absorption from the digestive tract of provitamin A and the fat-soluble vitamins A, D, and K, and consequently interferes with the utilization of calcium and phosphorus, with the result that the user is left liable to deficiency diseases." 21 C.F.R. 201.302(G)(a) (2018).

61. Due to the Advisory Committee's negative response to the ANCHOR trial, on October 16, 2013, the National Association of Securities Dealers halted trading in Amarin ADS's. Amarin Corporation plc, Historical Data, Yahoo! Finance, https://finance.yahoo.com/quote/AMRN/history?period1=1380600000&period2=1383278400&i nterval=1d&filter=history&frequency=1d (last visited July 7, 2019). Upon its resumption of trading on October 17, 2013, Amarin shares declined by an additional $3.16 per share from

$5.17 per share to $2.01 per share (an over 61% loss in value) on exceptionally high trading volume of 105.7 million shares. *See id.*

62. Shortly after the Advisory Committee Meeting took place, Amarin issued its quarterly financial report for the third quarter of 2013 in which it discussed the concerns with the placebo arm raised by the FDA during the meeting, stating, in relevant part:

> During the advisory committee meeting, based in part on the briefing materials prepared by the FDA for the meeting, the advisory committee reviewed the safety and efficacy data observed in the ANCHOR trial. This included a discussion regarding observed nominally statistically significant changes from baseline in an adverse direction, while on background statin therapy, in certain lipid parameters, including TGs, in the placebo group, ***raising the possibility that the mineral oil placebo used in the ANCHOR trial (and in the REDUCE-IT trial) was not biologically inert and might be viewed as artificially exaggerating the clinical effect of Vascepa when measured against placebo*** in the ANCHOR trial.

Amarin Corp. plc, Quarterly Report (Form 10-Q) 35 (Nov. 7, 2013).

63. Per the FDA's instructions during the Advisory Committee Meeting, Amarin directed the independent data monitoring committee for the REDUCE-IT trial "to periodically review unblinded lipid data to ***monitor for signals that the placebo might not be inert***" and to provide a recommendation as to whether the trial should continue as planned. Amarin Corp. plc, Quarterly Report (Form 10-Q) 43 (May 8, 2015).

E. The *Sklar* Class Action

64. As a result of the drops in Amarin's share price on October 11 and 16, 2013, on November 1, 2013, plaintiff Steven Sklar filed a class action in the United States District Court for the District of New Jersey against Amarin and then-CEO Zakrzewski for violations of Sections 10(b) and 20(a) of the Exchange Act and Rule 10b-5. *See* Complaint, *In re Amarin Corporation PLC, Securities Litigation*, 3:13-cv-06663-FLW-TJB (D. N.J. November 1, 2013) (the "***Sklar* Action**"), ECF No. 1.

65. On September 19, 2014, the court-appointed lead plaintiff filed an amended class action complaint adding Thero and Ketchum as defendants.[10] Consolidated and Amended Class Action Complaint, *Sklar* Action, ECF No. 52. The amended complaint contained several different allegations concerning the defendants' failure to disclose issues affecting the approval prospects of the ANCHOR indication that came to light in the FDA Briefing Document and during the Advisory Committee Meeting. *See generally*, *id.*

66. In one such allegation, the complaint claimed that the defendants misrepresented facts concerning issues presented by the mineral oil placebo in the ANCHOR trial. *Id.* at ¶¶72-85, 142-143. In support of this allegation, the amended complaint cited to the FDA's concerns expressed in the FDA's Briefing Document and during the Advisory Committee Meeting for the ANCHOR trial, as set forth in ¶¶51, 54-56 above. *Id.* at ¶¶ 78-82, 313. Additionally, the amended complaint included statements from a senior director of clinical research and medical affairs at Amarin (referred to as "Confidential Witness A" or "CWA") revealing that the mineral oil issues seen in the ANCHOR trial and their potential impact on the REDUCE-IT trial had been discussed internally at Amarin:

> In September 2011, Confidential Witness A ["CWA"], a senior director of clinical research and medical affairs at Amarin who reported to Paresh Soni, Senior Vice President, Head of Development, was concerned that the mineral oil placebo was not inert and had an adverse impact on the absorption of the statin, which resulted in the 8.8% increase in LDL-C and 5.9% increase in TG readings in the control arm. Soni informed [CWA] that he too was concerned that mineral oil was not inert and had discussed his concerns with defendant Zakrzewski. . . .
>
> Because of his concern with mineral oil as the placebo, [CWA] recommended to [] Soni and Rene Braeckman (Head of Development Operations) that Amarin

[10] Although not named as defendants in the *Sklar* Action, Granowitz joined Amarin as CMO in January 2016 while the Action remained ongoing and Joseph T. Kennedy, Amarin's current General Counsel, joined Amarin in December 2011, and thus served as General Counsel for the entirety of the *Sklar* Action. *See* Executive Team, Amarin Corporation, https://amarincorp.com/executive_team.html (last visited on July 12, 2019).

> conduct a . . . study to compare mineral oil placebo to corn oil and olive oil to determine if there were effects on results [and potentially modify the newer REDUCE-IT study]. Other similar studies of drugs with similar viscosity and taste to Vascepa at the time were using olive oil or corn oil placebos. Soni and Braeckman rejected any potential study or modifications to the REDUCE-IT protocol because the SPA had been approved by the FDA and the ANCHOR study had been conducted with mineral oil as the placebo. Zakrzewski told [CWA] that he would not allow any change to REDUCE-IT and that this study would meet a budget number and not to answer a scientific question and that Amarin 'was not moving backwards.' Zakrzewski told [CWA] that he was not changing any studies that would affect the time line of when Amarin could file the sNDA with the FDA for the ANCHOR indication.

Id. at ¶¶78-79.

67. Ultimately, on April 27, 2015, the FDA provided a Complete Response Letter ("**CRL**") to Amarin denying approval of the sNDA for the broader use of Vascepa based upon the ANCHOR indication. *See* Complete Response Letter from James P. Smith, MD, MS Deputy Division Director, Division of Metabolism and Endocrinology Products, FDA to Steven Ketchum PhD, President of Research and Development, Amarin Corp. plc (Apr. 27, 2015) (on file with the FDA). The CRL explained that the FDA decided to deny approval because, after other recent studies, it no longer believes that the reduction of triglycerides is a sufficient endpoint to measure the reduction of cardiovascular risk. *See id.* The FDA instructed Amarin that it will need to provide evidence that Vascepa reduces the risk of major adverse cardiovascular events (MACE) in patients at high risk for cardiovascular disease, who have residually high triglyceride levels and are on LDL-C statin therapy, and explained that "the final results from the REDUCE-IT trial could be submitted to satisfy this deficiency." *See id.* Thus, the REDUCE-IT trial remained Amarin's only hope for approval of Vascepa in a broader indication than the approved MARINE indication.

68. The *Sklar* Action made its way up to the Third Circuit Court of Appeals, which on May 23, 2017, issued an order affirming the District Court's dismissal of the Action. *See In re*

Amarin Corp. PLC Sec. Litig., 689 F. App'x 124 (3d Cir. 2017). Thus, Thero, Ketchum, Kennedy, and Zakrzewski were all actively opposing, and therefore aware of, the allegations in the *Sklar* Action regarding the mineral oil placebo as recently as 2017.

F. The REDUCE-IT Trial Wraps Up

69. In March 2018, patients commenced the last study visits for the REDUCE-IT trial. *See* Press Release, Amarin Corp. plc, Amarin Reports Last Patient Study Visit Has Occurred, an Important Step Towards Completion of REDUCE-IT™ Cardiovascular Outcomes Study (June 28, 2018). By the end of June 2018, Amarin announced that adjudication of all potential endpoints for the REDUCE-IT trial was nearing completion. *See id.* The Company explained that the final steps preceding completion include resolving remaining queries in the trial database. *See id.* Amarin elaborated that "[o]nce the REDUCE-IT database is locked, consistent with other outcomes studies, Amarin and a team of experts plan to confidentially review, and analyze the data" and will thereafter promptly announce the results. *Id.* The Company predicted that it should be able to announce the results at the end of the third quarter of 2018. *See id.*

70. On September 12, 2018, Amarin primed the market for the upcoming release of the REDUCE-IT trial results by announcing that the primary results had been accepted for presentation at the 2018 Scientific Sessions of the American Heart Association on November 10, 2018 (the "**AHA Conference**"). *See* Press Release, Amarin Corp. plc, REDUCE-IT™ Trial Primary Results Accepted for Presentation at 2018 Scientific Sessions of American Heart Association (Sept. 12, 2018). Amarin stated that acceptance "is based on the ability of REDUCE-IT to address a critical question in cardiovascular prevention. The AHA has reviewed the design of the REDUCE-IT study, however, they have not yet seen the results of the study."

Id. Amarin projected that it would be in a position to announce the results of the REDUCE-IT trial before the end of September 2018. *See id.*

V. DEFENDANTS MAKE MATERIALLY MISLEADING STATEMENTS

71. Two weeks later, on September 24, 2018, the Class Period began when Amarin announced the highly anticipated results of the REDUCE-IT trial. *See* Press Release, Amarin Corp. plc, REDUCE-IT™ Cardiovascular Outcomes Study of Vascepa® (icosapent ethyl) Capsules Met Primary Endpoint (Sept. 24, 2018). Amarin and the Officer Defendants reported that the REDUCE-IT trial met its primary endpoint because there was a 25% relative risk reduction, to a high degree of statistical significance ($p<0.001$), in major adverse cardiovascular events (MACE) in the intent-to-treat patient population with use of Vascepa 4 grams/day as compared to placebo. *Id.* In the press release announcing the results, Amarin, Thero, and Granowitz touted the outcome of the trial, stating, in relevant part the following:[11]

> Amarin Corporation plc (NASDAQ:AMRN), announced today topline results from the Vascepa® cardiovascular (CV) outcomes trial, REDUCE-IT™, a global study of 8,179 statin-treated adults with elevated CV risk. ***REDUCE-IT met its primary endpoint demonstrating an approximately 25% relative risk reduction, to a high degree of statistical significance (p<0.001), in major adverse CV events (MACE) in the intent-to-treat patient population with use of Vascepa 4 grams/day as compared to placebo***. . . .
>
> ***Efficacy: Approximately 25% relative risk reduction, demonstrated to a high degree of statistical significance (p<0.001), in the primary endpoint composite of the first occurrence of MACE***, including cardiovascular death, nonfatal myocardial infarction (MI), nonfatal stroke, coronary revascularization, or unstable angina requiring hospitalization. ***This result was supported by robust demonstrations of efficacy across multiple secondary endpoints***. . . .
>
> "We are delighted with these topline study results," said John F. Thero, president and CEO of Amarin. "Given Vascepa is affordably priced, orally administered and has a favorable safety profile, ***REDUCE-IT results could lead to a new paradigm in treatment to further reduce the significant cardiovascular risk that***

[11] Although many statements by Amarin and the Officer Defendants are listed in this section, the statements being challenged as false and/or misleading are those statements that are ***bolded, italicized, and*** in some instances ***underlined*** for emphasis.

remains in millions of patients with LDL-C controlled by statin therapy, as studied in REDUCE-IT."

"Considered against the backdrop of multiple unsuccessful cardiovascular outcomes studies of earlier generation drug therapies, including multiple recent failed cardiovascular studies of omega-3 mixture products that contain the omega-3 acid DHA, ***REDUCE-IT topline results stand alone as positive and confirm our hypothesis that pure EPA Vascepa at 4 grams/day can provide additional cardiovascular risk reduction benefit on top of LDL-C control with standard of care statin therapy in studied patients***," added Craig Granowitz, MD, PhD, senior vice president and chief medical officer of Amarin. "REDUCE-IT results cannot be generalized to fenofibrate, fish oil or omega-3 mixture products that contain DHA. The most relevant comparator study to REDUCE-IT is the Japan EPA lipid intervention study (JELIS), the 18,645 patient, open label, blinded endpoint outcomes study of EPA added to low-dose statin therapy, which showed cardiovascular event reduction in Japanese hypercholesterolemic patients of 19% in the overall population and 53% in a subgroup of patients with elevated TG levels and low HDL-C."

72. The Company also held a conference call that day to further exalt the results of the REDUCE-IT trial. Transcript of Vascepa REDUCE-IT Study Result Call (Sept. 24, 2018) (on file with Bloomberg). During the call, Amarin, Thero, Ketchum, and Granowitz stated in relevant part the following:

[Thero]: On this call, ***I'll recap topline results of REDUCE-IT and provide context on how these truly remarkable results fit within our current market dynamics and how they could affect demand for Vascepa generally***. I'll then hand the call over to Dr. Steve Ketchum, our President of R&D and Chief Scientific Officer, to provide more detailed context on the REDUCE-IT study itself. ***To recap REDUCE-IT results, approximately 25% relative risk reduction in the primary endpoint composite of the first occurrence of major adverse cardiovascular events known as MACE. That 25% is on top of LDL-C controlled by statin therapy in REDUCE-IT patients***. LDL-C controlled with statin therapy is generally understood to lower cardiovascular risk by 25% to 35%. ***Our REDUCE-IT result added approximately 25% cardiovascular risk reduction on top of the controlled LDL-C. That's huge, folks. That approximately 25% relative risk reduction was achieved to a high degree of statistical significance, p less than 0.001. This primary endpoint result was supported by robust demonstrations of efficacy across multiple secondary endpoints***. . . .

[Thero]: For perspective, note that the relative risk reduction of Lipitor, atorvastatin, is approximately 25%. Lipitor, before going generic, was one of the most successful branded drugs of all time and ***the 25% relative risk reduction***

from Vascepa in REDUCE-IT is 25% on top of statin therapy. This is indeed huge and represents a greater reduction than demonstrated on top of statin therapy for any other drug. It also positions Vascepa to be first to market in addressing a large unmet medical need. This is an extremely exciting result. ***This result appears to significantly exceed the expectations of even the highest degree of success scenarios projected by analysts covering Amarin over the years. We will strive to put these results in context today, so that models can be revised***. . . .

[Thero]: It's clear that management of LDL-cholesterol, known as bad cholesterol, is not enough. LDL-cholesterol management with statin therapy lowers cardiovascular risk by 25% to 35%. But this leaves 65% to 75% of residual risk. There is an urgent need to help reduce this residual risk. ***An additional 25% relative risk reduction in REDUCE-IT, on top of well-controlled LDL-cholesterol through statin therapy positions Vascepa as the single, most significant advance in preventative cardiovascular drug therapy since the advent of statin therapy***. That's a big statement. Let's pressure-test that statement now. Keep in mind, folks, decades of drug development in multiple drug classes has failed to significantly improve outcomes on top of standard of care statin therapy. . . . ***REDUCE-IT results with 25% relative risk reduction on top of statins are not only outstanding, but keep in mind, Vascepa is already viewed as a safe drug, an inexpensive drug and as a drug that already enjoys broad insurance coverage, as it has been on the market for five years***. . . .

[Thero]: Fast forward to over a decade and hundreds of millions of dollars of big pharma clinical development to REDUCE-IT. ***With approximately 25% relative risk reduction on top of statin therapy now demonstrated, we have confirmed that our easy-to-use drug that's inexpensive with broad reimbursement coverage significantly reduces cardiovascular risk. It thus has the potential to overcome the limitations of multiple blockbuster prior generation therapies. It thus has the potential to be a significant blockbuster and help millions of patients reduce cardiovascular risk on top of standard of care statin therapy***. . . .

[Thero]: I'll share one important aspect of that unique clinical profile with you now. It will help explain why REDUCE-IT results certainly cannot be generalized to any prior generation add-on to statin such as a fenofibrate and why the REDUCE-IT results cannot be generalized to common fish oil or omega-3 mixture products that contain the omega-3 acid DHA. Followers of Amarin are familiar with the Japanese EPA Lipid Intervention Study known as the JELIS study. JELIS is the most relevant comparator study to REDUCE-IT. It's an 18,645-patient open-label, blinded endpoint analysis cardiovascular outcome study of EPA, the same active ingredient in Vascepa added to low-dose statin therapy. ***JELIS showed cardiovascular event reduction in Japanese hypercholesterolemic patients of 19% in the overall population. And in a niche subgroup of patients with elevated triglyceride levels and low HDL cholesterol, a 53% relative risk reduction. That 19% relative risk reduction is comparable to***

the 25% in REDUCE-IT. Importantly, JELIS was a study of hypercholesterolemic patients. That is patients on low-dose statins but with high bad cholesterol. Persistent elevated triglyceride levels were not an entry criteria as they were in REDUCE-IT, and indeed, the median baseline triglyceride levels were not high in JELIS at 153 mgs per deciliter. . . .

[Thero]: More study was then needed to confirm such a benefit from EPA. And the FDA then encouraged us to complete REDUCE-IT to help answer that question. We are grateful for their prodding and delighted with the REDUCE-IT results. ***With an approximate 25% risk reduction on top of statin therapy, we're satisfied that we have confirmed Vascepa's unique characteristics and their utility in lowering cardiovascular risk in REDUCE-IT***. . . .

[Ketchum]: Moreover, I can't express enough appreciation to the clinical sites and patients involved in this important study. ***The topline results we are sharing today are, indeed, very positive and representative of an overall robust study result.*** We are very eager to share REDUCE-IT data in greater detail with both the medical and regulatory communities. . . .

[Ketchum]: The design of the REDUCE-IT study was robust. REDUCE-IT was designed to provide 90% power to detect a 15% relative risk reduction between arms. ***The highly statistically significant approximately 25% relative risk reduction in the primary outcome helps demonstrate that robustness, as does the robust demonstrations of efficacy across multiple secondary endpoints***. . . .

[Kethcum]: As announced with respect to the primary endpoint of the study, ***the key topline result of the REDUCE-IT study, as reported today, is approximately 25% relative risk reduction, demonstrated to a high degree of statistical significance P less than 0.001. This topline primary endpoint result is supported by robust demonstrations of efficacy across multiple secondary endpoints***. To preserve the ability to publish and to help move that process along quickly, we are not disclosing additional details of these secondary endpoints at this time. We reiterate, however, that ***the P value in this large multicenter trial was highly statistically significant at less than P 0.001, which is generally recognized as a statistically very persuasive finding. Results were supported by robust demonstrations of efficacy across multiple secondary endpoints***. . . .

[Ketchum]: Importantly, Vascepa's effect in the REDUCE-IT study is in patients with a median baseline LDL-C of 75 milligrams per deciliter. ***We view the approximately 25% relative risk reduction in the primary endpoint as particularly compelling in light of that low LDL-C level. 75 milligrams per deciliter for LDL-C is 25% lower than the target LDL-C historically recognized as a target for healthy adults.*** 75 milligrams per deciliter is very close to 70 milligrams per deciliter which is the historically recognized target level of LDL-C for at-risk patients. That is the level of LDL-C that doctors aim to achieve with statin therapy for patients that have other CV risk factors. So, keep in mind that

patients enrolled in REDUCE-IT had their LDL-C in control with statin therapy at the study start. Vascepa is not an LDL-C lowering therapy. ***The approximately 25% cardiovascular benefit demonstrated in REDUCE-IT was in addition to, that is on top of that achieved by statin LDL-C lowering and control.*** Likewise, while enrollment focused on patients with TGs between 150 milligrams to 499 milligrams per deciliter, median baseline TGs were 216 milligrams per deciliter. ***We view the approximately 25% relative risk reduction in the primary endpoint as particularly compelling in light of median TG levels in REDUCE-IT of 216 milligrams which is on the low end of the enrollment range***. . . .

[Granowitz]: And it's important for us to think about the fact that ***the secondary endpoints were robust across a large number of those endpoints***. ***And I think what the medical community is looking for is consistency of magnitude of effect. And that's what we've tried to communicate in the release is that the effects are consistent and robust across a wide range of these secondary endpoints in the study***.

[Thero]: But Craig is right, the consistency and the robustness of the data, I think, will be – ***this is a robust study. It's going to be very interesting to people.*** . . . The details of that further data, we are very excited about presenting the results at AHA, ***but 15% – excuse me, 25%; and I'd say 15%, that is our desire. If you move into this new paradigm, 25%, our relative risk reduction is huge and, I think to your point, it's going to draw a lot of attention at AHA***. So, hopefully, those comments are useful. . . .

[Thero]: We don't compete with PCSK9s, they're a lot more expensive, but at 15% relative risk reduction, the analysis of pharmacoeconomics suggests that the value of that therapy is higher than what is the current pricing of Vascepa. ***We have better – we have stronger relative risk reduction and a lower price and of course, we're also oral and we're really nice safety profile***. So, we'll look forward to seeing what analysis comes out of that. Number three, and all that information, we look forward to including in our presentation at American Heart Association. . . .

[Thero]: ***15% is viewed as a major winner and anything above that was sort of a dream.*** And we know that there's a bit of a paradox out there, right? Cardiovascular disease is the biggest area of death, bigger area in healthcare spending, but it's also an area where innovation has been slow in part because that's difficult. It also creates some barriers to somebody coming in behind us. But docs change behavior slower in this area than they do in some other areas, say oncology, for example. ***But this result is remarkable.*** Hopefully, it will catch their attention, we will see now as the data gets digested, presented public, just how well their behavior patterns change and whether that matches up to the research. ***But the research was pretty encouraging at 15% and 20% was really encouraging, so we'll see where that all goes. Obviously, 25% is what we achieved and that's the highest of any therapy, well higher than PCSK9, much more***

> ***affordable, but well higher than anything else that's out there. So, this should be a game changer***.

73. Notably during the conference call, Amarin and the Officer Defendants indicated that they had reviewed the entire data set, but explained that they were withholding the remaining results for the forthcoming AHA Conference presentation and a peer-reviewed journal article. *Id.* at 5-8, 10, 12. However, they assured the market that the remaining data was positive, showing "robust demonstrations of efficacy across multiple secondary endpoints." *Id.* at 5-6.

74. Also on September 24, 2018, Thero made an appearance on the CNBC show "Power Lunch" to discuss the results of the REDUCE-IT trial. CNBC, *Power Lunch: Amarin CEO on Future of Heart Drug Vascepa*, YouTube (Sept. 24, 2018), https://www.youtube.com /watch?v=rfDzakJJc7s. During the program, Amarin and Thero stated, in relevant part:

> [Thero at 00:00:06]: People have been working to lower cholesterol for years. We know that lowering cholesterol, whether it be through statins or PCSK9s, lowers cardiovascular risk by about 25 to 35 percent. 25 to 35 percent is terrific, but still of course leaves 60 to 75 percent residual risk. Where our drug is focused is addressing that 65 percent to 75 percent residual risk. ***So to be able to show 25 percent risk reduction on top of that cholesterol management is both new, and we believe very important in terms of an opportunity for improved healthcare***. . .
>
> [00:00:25]: A popup appears on CNBC's video that states: "***Approximately 25% relative risk reduction in heart disease patients with well-controlled LDL cholesterol***" . . .
>
> [00:01:23]: A popup appears on CNBC's video that states: "***25% reduction in risk of serious cardiovascular events***" . . .

75. Analysts were elated with this news. Jefferies raised its price target from $2.99 to $15.00 because "[t]he magnitude of MACE reduction is so far the greatest among all therapies on top of statins, far exceeding the clinically meaningful CV benefit expectation" and justifies "an opportunity to grow sales to $2-3" billion. Roger Song, *First-in-kind Positive CVOT:*

Vascepa REDUCEd CV Risks by 25%, Jefferies LLC (Sept. 24, 2018); Roger Song & Michael J. Yee, *Stock Has Room to Move Higher, Vascepa Potential SoC – Raising PT to $15*, Jefferies LLC (Sept. 24, 2018). In a report entitled "AMRN Has Landed The Whale[,]" Cantor Fitzgerald announced that it has raised its price target to $15.00 from $2.99 the day prior, explaining that the "REDUCE-IT results today could change the treatment paradigm for CV disease[.]" Louise Chen, et al., *AMRN Has Landed The Whale; Raising PT To $15 from $10 Post Positive Data*, Cantor Fitzgerald (Sept. 24, 2018). H.C. Wainright raised its price target from $10 to $20 because "Vascepa treatment on top of statin therapies wildly exceeded the skeptical consensus going into the data readout." Andrew S. Fein, et al., *REDUCE-IT Results Even Stronger than Our Best Case Scenario; Reit Buy and Raising PT to $20*, H.C. Wainright & Co. (Sept. 25, 2018).

76. The market's reaction mirrored the analysts' excitement. The share price soared from a close of $2.99 per share on September 23, 2018 to close at $13.00 per share on September 25, 2018, an increase of 433%. *See* Amarin Corporation plc, Historical Data, Yahoo! Finance, https://finance.yahoo.com/quote/AMRN/history?period1=1535774400&period2=1538712000&interval=1d&filter=history&frequency=1d (last visited June 28, 2019). Volume spiked from 4,265,400 shares on September 23, 2018 to 163,103,800 and 106,330,700 shares on September 24, 2018 and September 25, 2018, respectively. *See id.* The share price continued to rise in the following weeks, and reached the Class Period high of $22.98 per share on November 5, 2018, a 768% increase over the closing price on September 23, 2018.

77. In the following weeks Amarin and the Officer Defendants continued to tout the results of the REDUCE-IT trial at conferences and in Amarin's SEC filings.

78. On October 3, 2018 Thero gave a presentation at the Cantor Fitzgerald Global Healthcare Conference. *See* Transcript of Amarin Corporation PLC's CEO John Thero's Presentation at Cantor Global Healthcare Conference (Oct. 3, 2018) (on file with Seeking Alpha). During the presentation, Amarin and Thero stated in relevant part, the following:

> We know that cholesterol management is important but we know that cholesterol management only deals with a portion of the risk. Our solution is our lead product Vascepa which recently completed a landmark cardiovascular outcomes study, and ***I'll be going through those results during this presentation which includes a strong efficacy result***, as well as placebo like safety profile. ***This is the first successful outcome study in the space***. We'll talk a bit about why that is, and why that's different than what other products have done. . . .
>
> So before we had results from the study we spoke with our PI, we spoke with American Heart Association, we spoke with various journals who were interested in publishing this [indiscernible] type study and told them that we have to - we owe it to our stakeholders to describe some information in advance. They insisted that we hold back certain information for them. While, we have disclosed this on this slide and that is that we – that's the primary endpoint of the study which was again, relative risk reduction on that composite MACE endpoint that I described earlier. ***Our target had been 15% relative risk reduction, we achieved 25% relative risk reduction. And we did that with the p value which was statistically significant p less than 0.001. We also without providing quantification indicated that the underlying data is supportive of that primary result. We will have more to report on that that at the American Heart Association*** and our principal investigator, Deepak Bhatt from Brigham and Women's has expressed that he's very much looking forward to that presentation at the American Heart Association. . . .
>
> What has been shown to work is the one exception until our study reduced it was the JELIS study in Japan which also used EPA and show a 19% relative risk reduction, the drug has been very successful in Japan and it was hypothesis generating for what we're doing. ***We believe that the REDUCE-IT study is the definitive study conducted on global basis and that had the 25% relative risk reduction which, again, is a [indiscernible] statin level kind of relative risk reduction but this is on top of [indiscernible] statin and other statins***. . . .
>
> ***This is really a new paradigm that we're starting and we think it parallels that what we saw with statin therapy where you had earlier generation products*** whether it being Niacin in which hasn't succeeded in outcomes like various tolerability issues fenofibrates it also failed in outcomes studies to Lovaza or other Omega-3 mixtures which have failed in outcome studies. ***Now the new generation therapy which is different and that's Vascepa and with a 25%***

relative risk reduction on top of cholesterol management, we see this starting a new opportunity and hope it helps millions of people.

79. On November 1, 2018, Amarin published a press release to announce its third quarter financial results. *See* Press Release, Amarin Corp. plc, Amarin Reports Third Quarter 2018 Financial Results and Provides Update on Operations (Nov. 1, 2018). In the press release, Amarin and Thero stated, in relevant part, the following:

> The Vascepa® (icosapent ethyl) cardiovascular outcomes study, REDUCE-IT™, reported topline results on September 24, 2018. ***REDUCE-IT met its primary endpoint demonstrating an approximately 25% relative risk reduction, to a high degree of statistical significance (p<0.001), in major adverse cardiovascular events (MACE) in the intent-to-treat patient population with use of Vascepa 4 grams/day as compared to placebo***. Additional details regarding these important results are scheduled for presentation on November 10th at the 2018 Scientific Sessions of the American Heart Association (AHA) in Chicago, Illinois. . . .
>
> "***The landmark results of the REDUCE-IT study present an important opportunity to improve the practice of medicine with respect to preventative cardiovascular care. We believe that these outcomes study results position Vascepa to address a significant unmet medical need and could be considered the most significant breakthrough in preventative cardiovascular care since the advent of statin therapy decades ago.*** We are very excited about the potential for Vascepa to help millions of patients and we are acting accordingly to expand on our established commercial foundation, including existing broad managed care coverage and extensive key opinion leader support," stated John F. Thero, president and chief executive officer. "Amarin looks forward to the primary REDUCE-IT outcomes study results being presented at AHA and to working towards the future publication of these results in a major medical journal within 2018." . . .
>
> Until the AHA presentation, as agreed with AHA, Amarin does not plan to share any further details regarding the results of the REDUCE-It study***. Key topline results from the REDUCE-IT study as reported on September 24, 2018 include: Efficacy: Approximately 25% relative risk reduction, demonstrated to a high degree of statistical significance (p<0.001), in the primary endpoint composite of the first occurrence of MACE, including cardiovascular death, nonfatal myocardial infarction (MI), nonfatal stroke, coronary revascularization, or unstable angina requiring hospitalization. This result was supported by robust demonstrations of efficacy across multiple secondary endpoints***. No further information regarding the secondary endpoint results will be provided until the AHA presentation.

80. On that same day, Amarin filed its financial report for the third quarter of 2018 with the SEC on Form 10-Q. *See* Amarin Corp. plc, Quarterly Financial Report (Form 10-Q) (Nov. 1, 2018). The report was signed by Thero, with Amarin and Thero stating, in relevant part, the following:

> In September 2018, we announced landmark positive topline results of the REDUCE-IT cardiovascular outcomes trial. ***The REDUCE-IT study met its primary endpoint demonstrating an approximately 25% relative risk reduction in composite of major adverse cardiovascular events with high statistical significance. This result was supported by robust demonstrations of efficacy across multiple secondary endpoints***. The REDUCE-IT study results have been accepted for presentation at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018.
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> * * *
>
> **Item 1A. Risk Factors** . . .
>
> In September 2018, we announced topline results from the REDUCE-IT™ (Reduction of Cardiovascular Events with EPA—Intervention Trial) cardiovascular (CV) outcomes study of Vascepa. REDUCE-IT was a multinational, prospective, randomized, double-blind, placebo-controlled study, enrollment for which started in November 2011. REDUCE-IT investigated the effects of Vascepa on CV risk in statin-treated adults with well-controlled LDL-C 41-100 mg/dL (median baseline LDL-C: 75 mg/dL) and other CV risk factors, including persistent elevated TG 150-499 mg/dL (median baseline TG: 216 mg/dL). ***REDUCE-IT topline results showed the trial met its primary endpoint demonstrating an approximately 25% relative risk reduction, to a high degree of statistical significance (p<0.001), in major adverse cardiovascular events (MACE) in the intent-to-treat patient population with use of Vascepa 4 grams/day as compared to placebo***. MACE events were defined as a composite of cardiovascular death, nonfatal myocardial infarction (MI), nonfatal stroke, coronary revascularization, or unstable angina requiring hospitalization. ***This result was supported by robust demonstrations of efficacy across multiple secondary endpoints***. Vascepa was well tolerated in REDUCE-IT with a safety profile consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labelling. The proportions of patients experiencing adverse events and serious adverse events in REDUCE-IT were similar between the active and placebo treatment groups. Based on the final positive results of REDUCE-IT, we plan to seek additional indicated uses for Vascepa in the United States and to continue to develop Vascepa commercially in major markets around the world. . . .

> If Vascepa does not achieve an adequate level of acceptance, we may not generate product revenues sufficient to become profitable. ***The degree of market acceptance of Vascepa*** for the MARINE indication and in ANCHOR patients and ***in any future indications and uses based on the REDUCE-IT trial or otherwise will depend on a number of factors, including***: ***the perceived efficacy and safety of Vascepa by prescribing healthcare professionals, as compared to no treatment and as compared to alternative treatments in various at risk patient populations***, both as studied in clinical trials of Vascepa such as MARINE, ANCHOR and REDUCE-IT and not studied but for which the benefit/risk profile may be viewed as positive; . . .
>
> In September 2018, ***we announced topline results from the REDUCE-IT trial showing that the trial met its primary endpoint demonstrating an approximately 25% relative risk reduction, to a high degree of statistical significance (p<0.001), in MACE in the intent-to-treat patient population with use of Vascepa 4 grams/day as compared to placebo***. ***After announcement of favorable topline results from REDUCE-IT, additional data assessment and data release will yield additional useful information to inform greater understanding of study outcome.*** Generally, detailed trial data assessment may take several months and even years to complete and publish***. More detailed presentation of REDUCE-IT results are scheduled first at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018 in Chicago, Illinois. That presentation and additional data may exceed, match or may not meet investor expectations. Aspects that could change and impact the final evaluation of the totality of the efficacy and safety data from REDUCE-IT may include some or all of the following***: ***the magnitude of the treatment benefit on the primary composite endpoint, its components, secondary endpoints and the primary and secondary risk prevention cohorts***;

81. Along with the financial report, Amarin filed a certification pursuant to the Sarbanes-Oxley Act of 2002 signed by Thero which stated, in relevant part:

> Based on my knowledge, ***this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report***;

82. On November 1, 2018, Amarin also held a conference call to discuss its financial results from the third quarter of 2018. *See* Transcript of Amarin's Q3 2018 Earnings Call (Nov. 1, 2018) (on file with Bloomberg). During the conference call, Amarin and Thero stated, in relevant part, the following:

Even if Lovaza in VITAL surprises the medical community and in contrast to the body of evidence from other failed outcome studies of omega-3 mixtures, shows some level of cardioprotective benefit. ***It would be very surprising if the results approach anywhere near the approximate 25% risk reduction we reported for Vascepa top-line, REDUCE-IT cardiovascular outcome study results. We say this with confidence, because no other drug has demonstrated the ability to lower cardiovascular events by 25% on top of statin therapy***. . . . ***A recap of the-top line results we reported for REDUCE-IT study is as follows. Primary endpoint achieved with approximate 25% relative risk reduction in the composite of first occurrence of major adverse cardiovascular events, known as MACE. The 25% is on top of LDL cholesterol controlled by statin therapy in REDUCE-IT patients.*** LDL cholesterol controlled by statin therapy is generally understood to lower cardiovascular risk by 25% to 35%. ***Our REDUCE-IT results add approximately 25% cardiovascular risk reduction on top of controlled LDL-C. The top-line risk reduction of approximately 25% was achieved to a high degree of statistical significance, p less than 0.001. This primary endpoint top-line results were supported by robust demonstrations of efficacy across multiple secondary endpoints.*** We will not be providing more information regarding the secondary endpoint results until the presentation at AHA. On the safety side, Vascepa was well tolerated with a safety profile consistent with omega-3 fatty acids in current FDA-approved labeling. ***Cholesterol management lowers cardiovascular risk from 25% to 35%, leaving 65% to 75% residual cardiovascular risk. It is this substantial residual risk we seek to address with Vascepa. We believe that these clinical results position Vascepa to provide a new layer of cardioprotecive benefits which may potentially help millions of patients in the United States and internationally. Achieving 25% risk reduction on top of statin therapy is more than has been shown for any other therapy.*** For example, PCSK9s lower cardiovascular risk by 15%. ***Note that the risk reduction of the most widely used statin, Lipitor or atorvastatin, is approximately 25%, and Vascepa's 25% risk reduction is incremental to the benefit of statin therapy. Moreover, the REDUCE-IT results positions Vascepa to lead a new paradigm in patient care beyond cholesterol management. They also position Vascepa to be first-to-market in addressing a large unmet medical need***. . . .

Recall that in the JELIS study, the 19% risk reduction was achieved with only a 5% lowering of triglyceride levels. While elevated triglyceride levels are associated with higher levels of cardiovascular risks, it has not been established that lowering triglyceride levels alone significantly reduces cardiovascular risk. . .

We continue to reinforce that REDUCE-IT results are unique to Vascepa and cannot be generalized any prior generation add-on to statin, such as fenofibrates and that the REDUCE-IT results cannot be generalized to common fish oil or omega-3 mixture products, particularly those that can contain the omega-3 acid DHA. . . .

> ***It is flattering but not surprising to hear the accolades that outside advisors involved with the REDUCE-IT trial are repeatedly expressing regarding the high quality and ability of the Amarin's scientific team***. . . .
>
> ***We remain optimistic that the REDUCE-IT results will offshore in a new treatment paradigm to address the large unmet need of combating the residual risk of 65% to 75% that remain after statin treatment***. The market is potentially large as tens and millions of adults are at cardiovascular risk that cannot be addressed by cholesterol management alone. . . .
>
> ***This is with the REDUCE-IT results an opportunity to provide medical therapy that is a new paradigm in treatment*** that should really be thought of as very different than the market that dietary supplements are going after and dietary supplements try to cross over will take all actions appropriate to both educate and towards those efforts. . . .
>
> So, we are looking forward to presenting the results in detail at the American Heart Association, ***and we think that those details will be helpful to physicians in the end, I think the same people hopefully will remember it's a 25% reduction, but people seeing the results will give them confidence in the meaning of that 25%. So, hopefully, those comments were h[elp]ful***.

83. Amarin and the Officer Defendants' statements announcing the REDUCE-IT results on September 24, 2018, and in subsequently touting the results in the following weeks, set forth in ¶¶71-72, 74, 78-82 above, were misleading when made, in the context of the FDA's prior concerns regarding the impact of the mineral oil placebo in the ANCHOR trial, the FDA's rejection of the ANCHOR sNDA, the FDA's direction to Amarin to monitor the placebo arm in the REDUCE-IT trial, the allegations in the *Sklar* Action regarding the use of mineral oil as a placebo, Regulation 21 C.F.R. 201.302(G)(a) (2018), and recent failed cardiovascular studies of omega-3 products, because Amarin and the Officer Defendants omitted the following facts:

(a) In the Vascepa arm of the REDUCE-IT trial patients' median LDL-C derived[12] values increased from 74 to 77 mg/dL, or 3.1%, from baseline to

[12] The LDL-C values are characterized as "derived" and "Hopkins" based upon the two different methods that were used to calculate the levels. *See* NEJM Article supp. app. at 26.

the last visit, but in the placebo arm patients' median LDL-C derived values ***increased*** from 76 to 84 mg/dL, or ***10.2%***, from baseline to the last visit. *See* NEJM Article supp. app. at 38. Because properly performing statins should have kept LDL-C derived levels relatively constant from baseline, the increases in LDL-C derived levels in the placebo arm indicate that the mineral oil placebo may have interfered with patients' cholesterol-lowering statins. If the mineral oil had interfered with the statins in the placebo arm, the purported treatment effect, and thus the relative risk reduction, would have been far less significant than Amarin and the Officer Defendants initially reported, yet Amarin and the Officer Defendants failed to disclose this risk;

(b) In the Vascepa arm of the REDUCE-IT trial patients' median LDL-C Hopkins values decreased from 85.8 to 84 mg/dL, or 1.2%, from baseline to the last visit, but in the placebo arm patients' median LDL-C Hopkins values ***increased*** from 86.7 to 92.1 mg/dL, or ***6.5%***, from baseline to the last visit. *See id.* Because properly performing statins should have kept LDL-C Hopkins levels relatively constant from baseline, the increases in the LDL-C Hopkins levels in the placebo arm indicate that the mineral oil placebo may have interfered with patients' cholesterol-lowering statins. If the mineral oil had interfered with the statins in the placebo arm, the purported treatment effect, and thus the relative risk reduction, would have been far less significant than Amarin and the Officer Defendants initially

reported, yet Amarin and the Officer Defendants failed to disclose this risk;

(c) In the Vascepa arm of the REDUCE-IT trial patients' median Apo B values decreased from 82 to 80 mg/dL, or 2.5%, from baseline to the last visit, but in the placebo arm patients' median Apo B values ***increased*** from 83 to 86 mg/dL, or ***4.5%***, from baseline to the last visit. *See id.* Because properly performing statins should have kept Apo B levels relatively constant from baseline, the increases in Apo B levels in the placebo arm indicate that the mineral oil placebo may have interfered with patients' cholesterol-lowering statins. If the mineral oil had interfered with the statins in the placebo arm, the purported treatment effect, and thus the relative risk reduction, would have been far less significant than Amarin and the Officer Defendants initially reported, yet Amarin and the Officer Defendants failed to disclose this risk;

(d) In the Vascepa arm of the REDUCE-IT trial patients' median hsCRP[13] values decreased from 2.2 to 1.8 mg/L, or 12.6%, from baseline to the last visit, but in the placebo arm patients' median hsCRP values ***increased*** from 2.1 to 2.8 mg/L, or ***29.9%***, from baseline to the last visit. *See id.* Because properly performing statins should have kept hsCRP levels

[13] hsCRP is a protein released into the blood by the liver during inflammation, and thus is a commonly used clinical marker of general and cardiac-related inflammation. High Sensitivity C-Reactive Protein (hsCRP), ClevelandHeartLab (Sept. 2013), http://www.clevelandheartlab.com/wp-content/uploads/2013/09/hsCRP-Practitioner-One-Pager-CHL-D009b.pdf. Statins are used as a treatment to lower hsCRP levels. *See id.*

relatively constant from baseline, the increases in hsCRP levels in the placebo arm indicate that the mineral oil placebo may have interfered with patients' cholesterol-lowering statins. If the mineral oil had interfered with the statins in the placebo arm, the purported treatment effect, and thus the relative risk reduction, would have been far less significant than Amarin and the Officer Defendants initially reported, yet Amarin and the Officer Defendants failed to disclose this risk; and

(e) In the REDUCE-IT trial the mechanism(s) of action[14] responsible for the purported benefit observed in the Vascepa arm could not be identified. *See* NEJM Article at 20-21. The benefit could have been achieved from a host of different factors, including, but not limited to, a reduction in triglyceride levels, an antithrombotic mechanism of action, membrane stabilizing effects, stabilization or regression of coronary plaque, the difference in hsCRP, or a reduction in inflammation, but it was unclear which of these, if any, was the cause. *See id.* The fact that the mechanisms responsible for the benefit were unknown increases the likelihood that this result was just a fluke occurrence, creates the possibility that additional trials may be necessary to determine the mechanism(s) of action, and hinders doctors' ability to determine to which

[14] A "mechanism of action" is the biochemical process through which a drug produces its effect. Kristalyn Salters-Pedneault, P, *Mechanism of Action in Healthcare*, Verywell Mind (June 15, 2018), https://www.verywellmind.com/meaning-of-mechanism-of-action-in-health-care-425245.

patients the drug should be prescribed, thereby potentially reducing the adoption rate by physicians and the commercial prospects for Vascepa.

84. Despite being aware of these problems with the trial results, and aware that the FDA had previously been concerned with the mineral oil placebo in the ANCHOR trial, Amarin and the Officer Defendants decided to conceal this information from the market to drive up Amarin's share price and keep it inflated. Indeed, the Officer Defendants were personally motivated to keep these problems hidden because the Board of Directors had established a bonus incentive "Stretch Goal" for management, whereby they would earn 50% of their annual bonus if the REDUCE-IT trial achieved "20% or more in relative risk reduction" for the primary endpoint. *See* Amarin Corp. plc, Proxy Statement (Schedule 14A) 35 (Apr. 25, 2019). Furthermore, numerous insiders took advantage of the soaring share price and sold significant portions of their personal ADS holdings in the days after the announcement. *See* § VII.A.1 *infra*.

VI. RELEVANT POST-CLASS PERIOD EVENTS

A. The NEJM Article and AHA Presentation Disclose The Full REDUCE-IT Trial Results

85. On November 10, 2018, the New England Journal of Medicine ("**NEJM**") published an article written by Dr. Deepak L. Bhatt, the principal investigator for the REDUCE-IT trial, along with other trial investigators as well as Ketchum and Granowitz. The article was entitled "Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia" and featured the full results from the REDUCE-IT trial. *See* NEJM Article. In regard to the efficacy of Vascepa, the article explained that the drug showed a consistent benefit across the primary and secondary endpoints for the trial, stating, "[i]n the prespecified hierarchical testing of

[secondary] end points (Fig. 4), the rates of individual and composite ischemic end points[15] (except for death from any cause – the last secondary endpoint in the hierarchy) were significantly lower in the [Vascepa] group than in the placebo group, including the rate of cardiovascular death[.]" *See id.*

86. However, the article also disclosed for the first time the negative data from the REDUCE-IT trial that Amarin and the Officer Defendants had omitted from their prior discussions of the results beginning on September 24, 2018.

87. In regard to the issues with the placebo arm, the supplemental appendix to the article listed the lipid and lipoprotein biomarker results for the REDUCE-IT trial in a detailed chart, including the LDL-C derived, LDL-C Hopkins, Apo B, and hsCRP data points set forth in ¶83. As demonstrated in ¶83, the biomarker results show that, contrary to expectations, the LDL-C derived, LDL-C Hopkins, Apo B, and hsCRP levels for patients in the placebo arm increased by sizeable amounts during the trial. *See also* NEJM Article supp. app. at 38. The body of the article itself stated that "[t]he median change in LDL cholesterol level from baseline was an increase of 3.1% (2.0 mg per deciliter [0.05 mmol per liter]) in the [Vascepa] group and an increase of 10.2% (7.0 mg per deciliter [0.18 mmol per liter]) in the placebo group – a 6.6% (5.0 mg per deciliter [0.13 mmol per liter]) lower increase with [Vascepa] than with placebo (P<0.001)." NEJM Article at 16.

88. The article also acknowledged that the mechanism(s) of action responsible for the purported benefit seen in the Vascepa arm "***are currently not known***[,]" and elaborated that the

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[15] Ischemia is a restriction in blood supply to the tissues of the body, and myocardial ischemia occurs when blood flow to the heart is reduced, preventing the heart muscle from receiving enough oxygen. *See Myocardial Ischemia*, Mayo Clinic (Apr. 6, 2019), https://www.mayoclinic.org/diseases-conditions/myocardial-ischemia/symptoms-causes/syc-20375417.

data suggests "a delayed onset of benefit, which may reflect the time that is needed for a benefit from a reduction in triglyceride levels to be realized or may indicate that other mechanisms are involved." *Id.* at 21. The article set forth some possible mechanisms of benefit, positing that "modestly higher rate of bleeding events with [Vascepa] suggests that there may be an antithrombotic mechanism of action[,]" or "[i]t is possible that membrane-stabilizing effects could explain part of the benefit[,]" or "[s]tablization or regression of coronary plaque (or both) may also play a part[,]" or "[i]t is also possible that the difference in [hsCRP] level observed in REDUCE-IT may contribute to the benefit[.]" *Id.*

89. On November 10, 2018, Bhatt also presented the full results from the REDUCE-IT trial at the AHA Conference and largely reiterated the contents of the NEJM Article. *See* Deepak L. Bhatt, MD, MPH, et al., *Presentation at the 2018 Scientific Sessions of American Heart Association*, American Heart Association, (Nov. 10, 2018), *available at* https://aha.ondemand.org/aha/sessions/14120/view. During the presentation, Bhatt announced that the secondary endpoints, including the key secondary endpoint, showed statistically significant benefits in the Vascepa arm of the trial. *See id.* at 43. Bhatt also discussed some of the negative data from the REDUCE-IT trial.

90. First, Bhatt presented the data from baseline to the end of year 1 or year 2 for the key biomarkers in the trial (notably, the baseline to last visit levels were not included), including the LDL-C derived, Apo B, and hsCRP values. *See id.* at 18. Below is a copy of the slide with the biomarker data that Bhatt showed during his presentation, the relevant data is highlighted:

Effects on Biomarkers from Baseline to Year 1

	VASCEPA (N=4089) Median		Placebo (N=4090) Median		Median Between Group Difference at Year 1		
Biomarker*	Baseline	Year 1	Baseline	Year 1	Absolute Change from Baseline	% Change from Baseline	% Change P-value
Triglycerides (mg/dL)	216.5	175.0	216.0	221.0	-44.5	-19.7	<0.0001
Non-HDL-C (mg/dL)	118.0	113.0	118.5	130.0	-15.5	-13.1	<0.0001
LDL-C (mg/dL)	74.0	77.0	76.0	84.0	-5.0	-6.6	<0.0001
HDL-C (mg/dL)	40.0	39.0	40.0	42.0	-2.5	-6.3	<0.0001
Apo B (mg/dL)	82.0	80.0	83.0	89.0	-8.0	-9.7	<0.0001
hsCRP (mg/L)	2.2	1.8	2.1	2.8	-0.9	-39.9	<0.0001
Log hsCRP (mg/L)	0.8	0.6	0.8	1.0	-0.4	-22.5	<0.0001
EPA (µg/mL)	26.1	144.0	26.1	23.3	+114.9	+358.8	<0.0001

*Apo B and hsCRP were measured at Year 2.

Id.

91. Second, Bhatt also disclosed during the presentation that "[p]ending questions include that we cannot comment on the mechanisms of benefit from this study. While there was a consistent benefit across baseline and achieved triglyceride levels. Detailed biomarker and genetic analyses are planned." *See id.* The slide Bhatt showed when providing this explanation is set forth below:

Pending Questions

Cannot comment on mechanisms of benefit from this study

- Consistent reduction across triglyceride range (135-500)
- Similar benefit by 1-year triglycerides < or > 150 mg/dL
- Detailed biomarker and genetic analyses are planned

Cannot comment on cost-effectiveness

- Though with NNT of 21, likely cost-effective
- Formal cost-effectiveness analyses planned
- Full benefits not captured with only first events, await recurrent and total events analyses

Id. at 50.

92. Shortly after his presentation, Bhatt filmed a live video for the New England Journal of Medicine during which he spoke about the full results of the REDUCE-IT trial. During the video, Bhatt reiterated that they could not identify the mechanism(s) of action responsible for the purported benefit seen in the trial, stating:

> We've also got biomarker and genetic analyses—detailed analyses—planned, trying to get at what is the mechanism of benefit here. We saw reductions in triglycerides about 20 percent, we saw reduction in hsCRP about 22 percent, but the biggest change was in EPA levels, a 360 percent increase in EPA levels with the study group. So we're gonna try and tease apart, for the sake of science and future studies, what exactly drove the benefit on multiple endpoints in this trial.

Deepak L. Bhatt, MD, MPH, *Dr. Deepak Bhatt Discusses the REDUCE-IT Trial, Live From AHA 2018*, NEJMvideo (Nov. 10, 2018), *available at* https://www.youtube.com /watch?v=6NsUfLAy0DM.

B. The Market's Reaction To the Full REDUCE-IT Trial Results

93. In the aftermath of the November 10, 2018 AHA Conference and NEJM publication detailing the full REDUCE-IT trial results, observers were quick to raise concerns regarding the biomarker data in the placebo arm as well as the failure to identify the mechanism(s) of benefit.

94. A November 10, 2018 Forbes article raised questions regarding the full REDUCE-IT trial results and expressed the dismay of several leading cardiologists regarding the red flags in the data. Matthew Herper, *Amarin's Fish-Oil-Derived Drug Shows Great Promise—With Big Caveats*, Forbes Healthcare (Nov. 10, 2018), https://www.forbes.com/sites /matthewherper/2018/11/10/fish-oil-derived-drug-shows-great-promise--with-big-caveats/#2e715e0f3291 (the "**Forbes Article**"). Five out of six expert cardiologists surveyed in the Forbes Article were "seriously bothered" in the aftermath of the November 10, 2018

revelations because the results could have "exaggerate[ed] Vascepa's benefits" since "[t]he placebo that was given in the study appears to have caused blood test changes that might have caused heart attacks, potentially exaggerating the medicine's effectiveness." *Id.* Moreover, the experts cited in the Forbes Article were at a loss as to how Vascepa *actually* works. *Id.*

95. The Article focused first on the placebo's apparent impact on LDL-C and hsCRP:

> Patients who received mineral oil saw their levels of low-density lipoprotein, the bad cholesterol, increase 10% to 84 milligrams per deciliter, 6% more than in the Vascepa group, according to the New England Journal of Medicine paper. What's more, other blood test results used by cardiologists also went in the wrong direction. These changes were included in a supplement to the scientific paper, but not in the study itself. Levels of c-reactive protein, a measure of inflammation that is used to help calculate heart risk by some doctors, increased from 2.1 milligrams per liter to 2.8 milligrams per liter, a 30% increase.

Id.

96. In regard to the third biomarker, Apo B, the article stated:

> Stein says he is worried not just about LDL and CRP but about APO-B, another blood test that many lipid experts believe is as much a better predictor of cardiovascular risk. Median APO-B levels increased from 83 mg/dL to as high as 89 mg/dL. "My suspicion is that there is a benefit, but that it's much more mild than a first-line pass at the paper would suggest because of the harm in the placebo arm.

Id.

97. Dr. Harlan Krumholz, the Harold H. Hines, Jr. Professor of Medicine at Yale University, revealed that the results had caught most cardiologists by surprise, that the REDUCE-IT trial results could have been "a one-off chance finding[,]" and that he thought a second clinical trial would be needed to understand the result. *Id.*

98. Dr. Steven Nissen, chairman of cardiology at the Cleveland Clinic, explained that use of the mineral oil placebo was a "potential factor for driving the results that may result in an exaggeration of the benefits compared to what would be seen if there was a [true] placebo[.]" *Id.*

99. Dr. Ethan Weiss, a cardiologist at UC-San Francisco, explained that the REDUCE-IT trial results are "missing is a mechanism for what's going on in these biomarkers in the placebo side. They're all going in the wrong direction. You can't get beyond the argument that there's some biological mechanism of the placebo. *You can't say this is an inert placebo*." *Id.*

100. Dr. James Stein, the Robert Turell Professor of Medicine at the University of Wisconsin, took a drastically different view of the REDUCE-IT trial results after the November 10, 2018 revelations. *Id.* Initially believing that the REDUCE-IT trial results were a "home run" after the first set of results were announced in September 2018, he found that the new placebo revelations "turned it all on its head" and left him "really concerned" after assessing the placebo arm's biomarkers. *Id.*

101. Similarly, Dr. Sekar Kathiresan, director of the Cardiovascular Disease Initiative at the Broad Institute and the Center for Genomic Medicine at Massachusetts General Hospital, changed his opinion of the REDUCE-IT trial results after the November 10, 2018 revelations. Besides being worried about the placebo issue, Dr. Kathiresan expressed concern that the mechanism(s) behind Vascepa's ostensible benefit remains unexplained—especially given its reported magnitude. *Id.*

102. The Forbes Article concluded with an open question as to whether Amarin ought to have revealed significantly more to investors in its September 2018 press release, particularly about the placebo issue which so alarmed professional cardiologists. *See id.*

103. The following day, on November 11, 2018, the Company hosted a webcast to discuss the full data from the REDUCE-IT trial after the AHA Conference. *See* Transcript of Webcast Discussion of Primary REDUCE-IT™ Trial Results Following Presentation at 2018

Scientific Sessions of American Heart Association Call (Nov. 11, 2018) (on file with Bloomberg). During the webcast, the Company showed the same power point slides that Bhatt showed during his presentation, including the slides set forth in ¶¶90-91 *supra* which disclosed the negative biomarker results for the placebo arm and that the mechanism(s) of action responsible for the benefit could not be identified. Also during the webcast, Rebecca Juliano, Amarin's VP of Clinical Research & Development repeated that "we can't necessarily speak to exactly what the mechanism of action is in this study. I will note we have biomarker data that we have collected so we will do some interesting analyses and questions to try to get to that mechanism." *Id.*

104. The Company's webcast was followed by more critical commentary on November 11, 2018. An article entitled, "Amarin's REDUCE-IT Trial: Something Fishy?" was written by a retired cardiologist and published on investment website Seeking Alpha. *See* DoctoRx, *Amarin's REDUCE-IT Trial: Something Fishy?*, Seeking Alpha (Nov. 11, 2018), https://seekingalpha.com/article/4221035-amarins-reduce-trial-something-fishy. The article discussed at length the concerns raised by the by the biomarker results in the placebo arm which indicated that "the mineral oil may have harmed the health of the placebo[] group." *Id.* Specifically, the author noted:

> I am concerned that the placebo group received an active agent that in effect was an anti-statin, leading to an increase in LDL and CRP levels.
>
> The placebo contained mineral oil, a laxative, and the placebo group had more diarrhea, suggesting the placebo was active; the placebo group also had more anemia.
>
> Thus I posit that it's possible that the placebo was really a "placebo;" possibly the dramatic 25% reduction in MACE overstated the "true" effect[.]

Id.

105. As a result of the revelations of the aforementioned negative data at the AHA Conference and in the NEJM Article on Saturday, November 10, 2018, when Amarin's shares resumed trading on Monday, November 12, 2018, they began to decline over the course of two days, falling from a close of $21.05 per share on Friday November 9, 2018, to a close of $15.38 per share on Tuesday, November 13, 2018, a drop of $5.67 per share or 27%, on unusually high volume. *See* Amarin Corp. plc, Historical Data, Yahoo! Finance, https://finance.yahoo.com/quote/AMRN/history?period1=1541044800&period2=1543554000&interval=1d&filter=history&frequency=1d (last visited July 9, 2019).

VII. ADDITIONAL SCIENTER ALLEGATIONS

106. Defendants knew, or recklessly disregarded the risk that, the statements touting the results of the REDUCE-IT trial were misleading to Plaintiffs and the Class. Defendants acted with scienter by virtue of: (a) their opportunity and financial motives to commit fraud; (b) the fact that Vascepa was Amarin's core (in fact its only) product and the REDUCE-IT trial was vital to the Company's financial future; (c) their possession of and access to the full results from the REDUCE-IT trial—including the aberrations in the placebo arm—at the time the misleading statements were made; and (d) their knowledge and appreciation of the implications of the aberrations in the placebo arm of the REDUCE-IT trial data. These facts raise a compelling inference that Amarin and the Officer Defendants' misleading statements and omissions of material facts intentionally or recklessly deceived, defrauded, and misled investors about the strength of the REDUCE-IT trial outcomes and the Company's financial health.

A. The Individual Defendants Had the Motive and Opportunity To Commit Fraud

107. The Individual Defendants possessed the opportunity and financial motive to artificially inflate the price of Amarin shares, supporting the compelling inference of scienter.

The Individual Defendants stood to make a large sum of money if the results of the REDUCE-IT trial were positive, both through suspiciously timed, large ADS sales and through Amarin's executive compensation plan, which tied their remuneration directly to the trial's outcome.

1. Suspicious Insider Selling

108. While in possession of material, non-public information, during the Class Period, Ketchum sold over a million Amarin ADS's, representing 78% of his total holdings. Ketchum made these sales during the six-week period between when the first set of REDUCE-IT trial results were announced in September 2018 and when the full results were made public in November. Ketchum's significant and suspiciously timed sales made him over $8.3 million in profit and demonstrate that he knew the full results of the REDUCE-IT trial would diminish Amarin's share price.

109. As of September 24, 2018, the date the results were announced, Ketchum owned 400,473 shares of Amarin ADS's. After the announcement of the results, but before the full data was publicized on November 10, 2018, Ketchum exercised an option to acquire 1,153,711 shares of Amarin ADS's. While the ADS's were artificially inflated, he then sold 1,212,877 shares, realizing a gain of over $8.3 million. Ketchum thus sold the equivalent of 300% of his pre-Class Period holdings during the Class Period (or over 78% of his total holdings at the time of the sales).

110. Ketchum's ADS sales during the Class Period were unusual in size and timing. Indeed, Ketchum sold *no* shares at all during the 47 days preceding the Class Period.[16] And for all of 2018 prior to the Class Period, Ketchum sold only 388,185 shares, significantly less than his Class Period sales. Ketchum sold only 63,479 shares of Amarin stock in 2017 and *no* shares

[16] The Class Period, from September 24, 2018 through and including November 9, 2018, totals 47 days.

at all in 2016. The profit Ketchum realized—over $8.3 million—was also unusual compared to his base compensation of $462,300. *See* Amarin Corp. plc, Proxy Statement (Schedule 14A) 28 (Apr. 25, 2019).

111. Zakrzewski also made a large and unusual stock sale during the Class Period. While in possession of material, non-public information, Zakrzewski sold half a million Amarin ADS's, representing over 68% of his total holdings. Zakrzewski made these sales during the six-week period between when the first set of REDUCE-IT trial results were announced in September 2018 and when the full results were made public in November. Zakrzewski's significant and suspiciously timed sales made him $3.6 million in profit and demonstrate that he knew the full results of the REDUCE-IT trial would diminish Amarin's share price.

112. As of September 24, 2018, the date the first results were announced, Zakrzewski owned 226,047 shares of Amarin ADS's. After the first announcement of the REDUCE-IT trial results in September 2018, but before the full results were publicized in November, Zakrzewski exercised an option to acquire 500,000 shares of Amarin ADS's. While the ADS's were artificially inflated, he then sold all 500,000 shares, realizing a gain of over $3.6 million. Zakrzewski thus sold the equivalent of 200% of his pre-Class Period holdings during the Class Period (or over 68% of his total holdings at the time of the sales).

113. Zakrzewski's ADS sales during the Class Period were unusual in size and timing. Zakrzewski sold *no* shares at all in 2018 prior to the Class Period. Additionally, Zakrzewski's sale made him $3.6 million in profit, many times more than the $60,000 he made in compensation as a member of Amarin's Board of Directors.

114. While in possession of material, adverse information, Defendant Thero sold 622,368 shares of Amarin ADS's. Thero made these sales during the six-week period between

when the first set of REDUCE-IT trial results were announced in September 2018 and when Amarin's stock price substantially declined a result of the disclosure of the full results in November. Thero's significant and suspiciously timed sales made him more than $11.27 million in profit and demonstrate that he knew the full results of the REDUCE-IT trial would diminish Amarin's share price.

115. Thero's ADS sales during the Class Period were unusual in size and timing. Thero sold 497,876 shares during the 47 days prior to the Class Period, for a profit of only $1,488,649.24, far less than the more than $11 million he made before the stock price declined on November 12-13, 2018. Thero also made over 16 times more than his 2018 base compensation of $664,800 in a single day.

116. Other high-level Amarin executives made suspiciously timed, large ADS sales during the Class Period as well.

117. Joseph T. Kennedy, Amarin's General Counsel, owned 217,934 shares on September 24, 2018. He exercised an option to acquire 1,179,757 shares during the Class Period and sold them all—over 84% of his total holdings—making over $10.6 million in profit.

118. Kennedy's ADS sales during the Class Period were unusual in size and timing. Kennedy sold *no* shares at all during the 47 days prior to the Class Period. And for all of 2018 prior to the Class Period, he sold only 263,150 shares for profits of $928,483—substantially less than his Class Period sales.

119. Michael Wayne Kalb, Amarin's Chief Financial Officer, sold 150,000 shares—over 90% of his total holdings—during the Class Period, realizing $1.2 million in profit.

120. Kalb's ADS sales during the Class Period were unusual in size and timing. He sold *no* shares at all during the 47 days prior to the Class Period. And for all of 2018 prior to the

Class Period, he sold only 14,404 shares for profits of $53,635—substantially less than his Class Period sales.

121. At the same time Amarin and the Officer Defendants were telling investors that the REDUCE-IT trial was an unqualified success and concealing material information to the contrary, Thero, Ketchum, Zakrzewski, and other Amarin executives offloaded over three million shares of Amarin ADS's, banking over $34 million in profit, all before Amarin's share price declined as a result of the announcement of the full data from the REDUCE-IT trial. These sales support the compelling inference that Amarin intentionally withheld material information about the REDUCE-IT trial results to artificially inflate Amarin's share price, defrauding investors such as Plaintiffs and Class members.

2. Amarin's Executive Compensation Plan

122. Several of the Officer Defendants were also motivated to commit fraud with respect to the REDUCE-IT trial results to enhance their executive compensation.

123. As Amarin executives, Thero's and Ketchum's compensation was directly linked to the success of the REDUCE-IT trial. In addition to awards of stock options, Amarin's Executive Compensation Plan incentivized executives through cash bonuses. In 2018, Amarin executives, such as Thero and Ketchum, were promised a cash bonus equivalent to 50% of their salary if the REDUCE-IT trial achieved a 20% or higher relative risk reduction for its primary endpoint, pursuant to a "Pre-Specified 'Stretch' Goal." Amarin Corp. plc, Proxy Statement (Schedule 14A) 35 (April 25, 2019).

124. According to Amarin's 2019 Proxy Statement, Amarin's Board of Directors approved four categories of "2018 Corporate Goals," and relative weighting, for purposes of calculating executive cash bonuses: "Commercial (40%); "Quality & Supply (10%)"; "Financial

and Public Relations/Investor Relations (20%)"; and a goal tied to finalizing and publishing the results from the REDUCE-IT trial, weighted at 30% of base salary. *Id.*

125. In addition, the Board set a "Pre-Specified 'Stretch' Goal: REDUCE-IT: Achieve 20% or more in relative risk reduction for primary endpoint," weighted at 50% of the executive's base salary. *Id.*

126. Thero received a $249,300 cash bonus award in connection with the Company's "achievement of the pre-defined REDUCE-IT stretch goal," and $473,670 in connection with the 2018 Corporate Goals. *Id.* at 37.

127. Ketchum received a $92,460 cash bonus award in connection with the Company's "achievement of the pre-defined REDUCE-IT stretch goal," and $177,986 in connection with the 2018 Corporate Goals and his individual goals. One of Ketchum's individual goals was to "[w]ork with REDUCE-IT steering committee and medical affairs team to secure publication of REDUCE-IT results in top-tier journal in parallel with late breaker presentation in the fourth quarter of 2018." *Id.* Achievement of this goal would necessarily have required Ketchum to review the data he was tasked with publishing.

B. Vascepa Is Amarin's Core and Only Product

128. Amarin sells a single product: Vascepa. As Amarin has acknowledged in its public filings, the Company relies on Vascepa as its "lead product." Amarin Corp. plc., Annual Report (Form 10-K) 2 (Feb. 27, 2019); *see also id.* at 6 ("Since our inception, we have devoted substantial resources to the research and development of Vascepa (icosapent ethyl) capsules.").

129. Amarin's main growth strategy has always been to market its single product to a larger patient population. At the time Amarin undertook the REDUCE-IT trial, Vascepa was (and still is) approved for a single indication, to lower triglyceride levels in people with severe hypertriglyceridemia. Roughly 4 million people in the United States have severe

hypertriglyceridemia, so with this single indication, Vascepa is marketable to a patient population of about 4 million persons domestically. *See* Amarin Corp. plc, Current Report (Form 8-K) (July 27, 2012). By way of comparison, one in four people in the United States have high (but not very high) cholesterol. If it could portray Vascepa as useful for improving outcomes for high cholesterol patients, Amarin would have access to a potential patient population of over 70 million people in the United States—approximately 17 times larger than its current market. *See* Press Release, Amarin Corp., plc, Amarin Commences 2012 with Letter to Shareholders (Jan. 3, 2012).

130. Beginning with the ANCHOR trial in 2011, Amarin set its sights on the population of tens of millions of people with high cholesterol. But after the ANCHOR trial results failed to convince the FDA to approve Amarin's application for an expanded indication for Vascepa, the REDUCE-IT trial was the key to accessing this exponentially larger patient population. Amarin sought not only to obtain FDA approval, but also to convince physicians and the public that Vascepa would be highly effective at improving cardiac outcomes for high cholesterol patients.

131. Amarin's future success was thus highly dependent on the results of the REDUCE-IT trial.

132. The REDUCE-IT trial was massive in both expense and scope. The Company expended $35 to $60 million annually to complete the trial—a significant sum for a company with approximately $180 million in annual revenue in 2017. *See* Amarin Corp. plc, Annual Report (Form 10-K) 61 (Feb. 27, 2018). In total, the REDUCE-IT trial cost over $300 million to perform. *See* Amarin Corp. plc, Current Report (Form 8-K) (Nov. 13, 2018).

133. Amarin had never undertaken a study of Vascepa anywhere near the size or scope of the REDUCE-IT trial. The two previous studies, MARINE and ANCHOR had lasted twelve weeks; the REDUCE IT trial took over eight years. ¶¶37, 42, 45. Amarin had also hyped the REDUCE-IT trial and its potential for the Company to investors for years.

134. In short, the future financial prospects of the Company were riding on the outcome of the REDUCE-IT trial. The Individual Defendants, as executives and directors at the Company were actively involved in and aware of the details of the pivotal trial. The Company's executives, including Thero, Ketchum, and Granowitz, discussed this information in press releases and on conference calls with analysts and investors.

135. As CEO, Thero was responsible for, and exercised control over, the Company. Thero was the Company's President and CFO from November 5, 2009 through December 2013. On January 1, 2014, he replaced Zakrzewski as CEO. Thero thus knew of Amarin's financial prospects and drug development activities, and spent years speaking on behalf of Amarin to the investing public about Amarin's financial status as well as the Phase 3 trial program for Vascepa. *See* Amarin Corp. plc, Proxy Statement (Schedule 14A) 5, 7 (Apr. 20, 2018).

136. Ketchum has been the Company's Senior Vice President and President of Research and Development since February 2012 and Amarin's CSO since January 2016. According to the employment agreement between Amarin and Ketchum dated February 12, 2012, he was an executive officer responsible for Amarin's research and development efforts. As the Company's Senior Vice President, President of Research and Development, and CSO he spoke on behalf of Amarin to the investing public providing information on matters relating to research and development, including Amarin's progress in the development and testing of Vascepa, and was the principal liaison with the FDA.

137. Granowitz has been the Company's Senior Vice President and CMO since January 2016. As the Company's Senior Vice President and CMO he spoke on behalf of Amarin to the investing public providing information on matters relating to research and development, including Amarin's Phase 3 trial program of Vascepa.

138. Zakrzewski was Amarin's CEO from November 2010 to December 2013 and has been a member of Amarin's board of directors since January 2010. By virtue of his position as CEO in 2013, Zakrzewski was aware of the issues raised by the FDA regarding the placebo arm in the ANCHOR trial, and by virtue of his role as a named defendant, Zakrzewski was aware of the allegations in the *Sklar* Action. As a director during the Class Period, Zakrzewski was responsible for overseeing Amarin's finances and operations, including any important developments in the clinical trial program for the Company's only product.

C. Defendants Had Analyzed the Full Data Set from the REDUCE-IT Trial by the Time Amarin Announced the Trial's Results on September 24, 2018

139. As described above, publicizing only the efficacy results that claimed a 25% reduction of major adverse cardiovascular events on top of statin therapy was false and misleading. The full dataset revealed important information that contradicted and provided important qualification as to that claim, including that: (1) the full REDUCE-IT data revealed no causal connection between Vascepa lowering triglyceride levels and the purported cardiac benefits—this meant it was simply "not known" how Vascepa could be generating positive efficacy results, and Amarin could not explain how its product worked without resorting to speculation about alternative causal mechanisms, increasing the likelihood that the result was just a fluke occurrence, indicating further studies would be needed to determine the mechanism of action, and hindering doctors' ability to prescribe the drug, thereby potentially reducing the adoption rate by physicians and the commercial prospects for Vascepa; and (2) the mineral oil

placebo may have caused the LDL-C derived, LDL-C Hopkins, Apo B, and hsCRP levels for patients in the placebo arm to increase by sizeable amounts during the trial, thereby potentially raising the rate of major cardiovascular events in the control group and thus exaggerating Vascepa's efficacy—at the very least, it called into question the proclaimed results of a 25% in cardiac outcomes.

140. As of September 24, 2018, when Amarin and the Officer Defendants announced the REDUCE-IT trial's efficacy results, Defendants had already analyzed the full REDUCE-IT trial data and thus knew that publicizing the results without important caveats would likely mislead investors. Defendants nevertheless chose to conceal from investors the key qualifying information contained in the full data.

141. By virtue of their positions and responsibilities at the Company, the Individual Defendants had access to the full analyzed data as soon as it was completed—days or weeks before the announcement on September 24, 2018.

142. Indeed, in June 2018, the Company explained that it maintains a central, internal database that contains a compilation all of the REDUCE-IT trial data. ¶69. At that time, the Company disclosed that once the trial data in the database has been fully synthesized, "Amarin and a team of experts plan to confidentially review, and analyze the data" before it is announced to the public. *Id.*

143. Amarin and the Officer Defendants' public statements confirm that the Company had the full data when Amarin announced the results on September 24, 2018.

144. As CSO, Ketchum had the full analyzed data from the REDUCE-IT trial as soon as it was available. Ketchum was the internal lead in charge of the REDUCE-IT trial, and supervised the team responsible for preparing the data for presentation. Ketchum was thus one of

the first, if not the first, Amarin employee (in addition to Thero, Amarin's CEO) to obtain the full results. Ketchum said as much on a conference call on September 24, 2018, when he touted the "very positive" results and said they were "representative of an overall robust study result" and said "[w]e are very eager to share REDUCE-IT data in greater detail with both the medical and regulatory communities." Transcript of Vascepa REDUCE-IT Study Result Call (Sept. 24, 2018) (on file with Bloomberg).

145. During that same conference call, Thero and Ketchum indicated that they had reviewed the entire data set, but explained that they were withholding the remaining results for the forthcoming AHA Conference presentation and a peer-reviewed journal article. *Id.* at 5-8, 10, 12. This included statements to the effect that the Company was not yet "disclosing additional details," and that they would not yet "talk too much about the results of the REDUCE-IT study because we are saving those further details for presentation." *Id.* at 6, 10-11. Yet they assured the market that the remaining data was positive, showing "robust demonstrations of efficacy across multiple secondary endpoints." *Id.* at 5-6.

146. Thero made similar statements during a presentation at the Cantor Fitzgerald Global Healthcare Conference held on October 3, 2018, indicating that while Defendants had access to the full data, they were not ready to share it with the public:

> "So before we had results from the study we spoke with our PI, we spoke with American Heart Association, we spoke with various journals who were interested in publishing this [indiscernible] type study and told them that we have to - we owe it to our stakeholders to describe some information in advance. ***They insisted that we hold back certain information for them***. While, we have disclosed this on this slide and that is that we – that's the primary endpoint of the study which was again, relative risk reduction on that composite MACE endpoint that I described earlier. Our target had been 15% relative risk reduction, we achieved 25% relative risk reduction. And we did that with the p value which was statistically significant p less than 0.001. ***We also without providing quantification indicated that the underlying data is supportive of that primary result. We will have more to report on that that*** [sic] at the American Heart Association and our principal investigator,

> Deepak Bhatt from Brigham and Women's has expressed that he's very much looking forward to that presentation at the American Heart Association."

Transcript of Amarin Corporation PLC's CEO John Thero's Presentation at Cantor Global Healthcare Conference (Oct. 3, 2018) (on file with Seeking Alpha) (emphasis added).

147. During the question and answer portion of the presentation, Thero made clear that he and the Company had more information than they were releasing publicly, encouraging analysts to "pay attention at AHA." *Id.*

148. On a conference call on November 1, 2018, Thero again touted the results while acknowledging that the Company had a fuller set of data that it was not yet sharing publicly: "[W]e are looking forward to presenting the results in detail at the American Heart Association, and we think that those details will be helpful to physicians in the end, I think the same people hopefully will remember it's a 25% reduction, but people seeing the results will give them confidence in the meaning of that 25%." Transcript of Amarin's Q3 2018 Earnings Call (Nov. 1, 2018) (on file with Bloomberg).

149. Amarin and the Officer Defendants' statements revealing that they already had the fuller set of data before publicizing the results are consistent with basic facts about clinical study results and the corresponding data analysis. In order to calculate the results that they ultimately published, Defendants necessarily would have had to look at and analyze a variety of data from the study, including from the placebo group. Considerable review, analysis, and calculations of the underlying data is necessary, in other words, to generate the results that Amarin and the Officer Defendants ultimately chose to publicize.

150. Notwithstanding any statements to the contrary by Thero, Ketchum, and others inside the Company, the New England Journal of Medicine does not have an editorial policy prohibiting verbal disclosures of information about a study's results before a related article is to

be published in the journal. Alex Lombino, Senior Editorial Assistant at the New England Journal of Medicine confirmed this point in a telephone conversation, saying that the Journal's embargo policy prohibits authors from providing ***written*** materials about the trial's results before the publication in the Journal. Lombino said the Journal's policy does not embargo verbal communications about trial results and that doctors are permitted to discuss and present any of the results of the trial before the publication.

151. As well, under the AHA's embargo policy, a company may release information about a study prior to the embargo if it notifies AHA in advance regarding the legal rationale for disclosing the information and explains to whom and how the information would be released. Embargo Policy, American Heart Association, https://newsroom.heart.org/policies/embargo-policy#ineligible (last visited July 18, 2019). AHA then will determine whether the study shall remain on the program of an AHA meeting or be published in an AHA scientific journal. *Id.* Thus, while Amarin and the Officer Defendants could have easily followed the aforementioned procedures to disclose the placebo and mechanism of action data on September 24, 2018, they were instead motivated to conceal the negative data in order to prevent AHA from cancelling the Scientific Sessions presentation. As detailed above, Amarin and the Officer Defendants had multiple opportunities to provide the necessary qualifications to avoid misleading investors yet chose not to do so.

152. At the very least, had Defendants not reviewed the full dataset about which they spoke at length during the Class Period, they were deliberately reckless in making statements about such data when they could have easily reviewed it in the database to which they had access.

D. Defendants Knew that Publicizing Only Limited Results Would Provide Incomplete and Misleading Information to Investors

153. There can be little doubt that Defendants knew the importance of (i) the lack of an explained causal mechanism for Vascepa improving cardiac outcomes; and (ii) the use of a non-inert placebo that, among other things, raised the LDL cholesterol in the control arm patients.

154. Amarin and the Officer Defendants' choice to discuss these issues in the first public presentation of the full REDUCE-IT trial at the AHA Conference on November 10, 2018, confirms that Defendants were aware they were important.

155. At the Conference, the presenters raised the issues affirmatively and included them in the investor slides that accompanied the presentation. Without prompting, Rebecca Juliano, Amarin's Vice President of Clinical Research and Development conceded, "we've had mineral oil questions really from our early days of the ANCHOR study." Transcript of Amarin Presentation of REDUCE-IT Trial Results at the American Heart Association Conference, November 10, 2018 (on file with Bloomberg) at 8. This is consistent with Ketchum's statement back in October 16, 2013, quoted above, acknowledging in the aftermath of the ANCHOR study that "the possibility of some type of inhibition of statin absorption" by the mineral oil placebo is "***obviously important***." *Supra* ¶57.

156. At the AHA Conference, Juliano also affirmatively revealed that Amarin could not explain the mechanism by which Vascepa lowered MACE, admitting, "we can't necessarily speak to exactly what the mechanism of action is in the study." Transcript of Amarin Presentation of REDUCE-IT Trial Results at the American Heart Association Conference, November 10, 2018 (on file with Bloomberg) at 9.

157. The presentation's focus on these major qualifications were consistent with the publication of the full results in the New England Journal of Medicine. Although the article

contained a wide variety of data points in the results, the authors chose to focus in particular on "certain limitations" of the trial, including that "if mineral oil in the placebo affected statin absorption in some patients, this might have contributed to differences in outcomes between the groups." NEJM Article at 21.. The article also highlighted the fact that the lower risks of cardiac events seen in those on Vascepa "appeared to occur irrespective of the attained triglyceride level … which suggests that the cardiovascular risk reduction was not associated with attainment of a more normal triglyceride level." *Id.* In other words, there was no indication that the improved patient outcomes were resulting from the mechanism by which Amarin believed Vascepa functioned. As the article put it, "Mechanisms responsible for the benefit of icosapent ethyl [Vascepa] observed in REDUCE-IT are currently not known." *Id.*

158. Consistent with both the Company's recognition that these issues needed to be addressed, and the article's authors' recognition that these issues needed to be addressed, the Forbes Article (discussed in ¶¶94-102 *supra*) published the same day noted that five out of six cardiologists interviewed about the full REDUCE-IT results were "seriously bothered" by the fact that the mineral oil given to the control group "had not behaved as a placebo at all." Matthew Herper, *Amarin's Fish-Oil-Derived Drug Shows Great Promise—With Big Caveats*, Forbes Healthcare (Nov. 10, 2018), https://www.forbes.com/sites /matthewherper/2018/11/10/fish-oil-derived-drug-shows-great-promise--with-big-caveats/#2e715e0f3291. Rather, as the doctors noted, the patients who received the mineral oil saw a 10% increase in their LDL levels—6% more than in the Vascepa group. Other indicators of heart health risks, hsCRP and Apo-B levels, also went up by statistically significant amounts in the control group, leading cardiologists to change their position from positive about Vascepa to having doubt. The cardiologists worried that the biomarkers in the control group were "all

going in the wrong direction," which lead the article's author to wonder: "Could the placebo be causing some heart problems or strokes, making Vascepa look better than it really is?"

159. Although some cardiologists interviewed by Forbes about the REDUCE-IT results characterized the top line results as just "an exaggeration of [Vascepa's] benefits compared to what would be seen if there was a [true] placebo," others who had been "floored" by the 25% relative risk reduction announced in the top-line results, said the placebo issue "turned it all on its head." *Id.*

160. After looking at the full REDUCE-IT data (for only one day), the cardiologists quoted in the Forbes Article also worried about the confusion surrounding how Vascepa actually works. Harlan Krumholz, a professor of medicine at Yale University, said he thought a second clinical trial would be needed to understand the results. Another physician, Ethan Weiss, a cardiologist at UC-San Francisco, said, "what we're missing is a mechanism for what's going on in these biomarkers in the placebo side. They're all going in the wrong direction. You can't get beyond the argument that there's some biological mechanism of the placebo. You can't say this is an inert placebo."

161. Nor was the mineral oil placebo concern new for Amarin. The FDA had scrutinized Amarin's use of the mineral oil placebo for years. *See* ¶¶50-56, 63 *supra*. The FDA had previously raised this issue with Amarin in connection with the earlier ANCHOR trial. *See* Transcript of Endocrinologic and Metabolic Drugs Advisory Committee Meeting (Oct. 16, 2013) (on file with the FDA). Early in the REDUCE-IT trial, the FDA had even gone so far as to direct investigators conducting the trial to monitor for signals that the mineral oil placebo might not be inert, which they did quarterly. *Id.* at 140-141.

162. Consistent with the above, Thero and Ketchum were advised years earlier by the FDA during the ANCHOR trial that mineral oil may not be biologically inert. In connection with the ANCHOR trial there were discussions about whether the use of a mineral oil placebo could artificially exaggerate the clinical effect of Vascepa. Ketchum had first-hand knowledge of the potential ramifications that aberrations in the placebo arm could have with the FDA, as he was primarily responsible for liaising with the FDA during the ANCHOR trial. Ketchum also participated in a 2013 hearing with the FDA in connection with the ANCHOR trial during which several FDA commissioners raised concerns that the mineral oil placebo was not inert and ultimately voted not to approve the expanded indication for Vascepa. *See id.*

163. Concerns about Amarin's use of mineral oil as a placebo thus materialized following each significant achievement with Vascepa. In 2013, in connection with the ANCHOR trial, the FDA briefing documents raised questions about the mineral oil placebo used in the ANCHOR trial intended to support the expanded approval, thereby potentially negatively impacting the control group data, and suggesting that "the treatment effects observed with [Vascepa] may be overestimated." *See* Mineral Oil and Inertness Issue, EPA Drug Initiative, http://epadruginitiative.com/files/Mineral_Oil_and_Placebo_Inertness_Issue.pdf (last visited July 22, 2019).

164. Thero and Ketchum were all executives with the Company at the time of the ANCHOR study and the prior securities class action was filed in this District alleging various false statements to investors surrounding Vascepa, including statements regarding the use of mineral oil placebo in the ANCHOR trial. Granowitz joined the Company a year before the case was finally dismissed. That case included allegations that witnesses at Amarin involved in the ANCHOR trial brought the aberrations to the attention of executives at Amarin, including the

Head of Development and the Head of Operations. The witness was told that Amarin would not change the study because the budget and timeline were more important than scientific integrity. In its Briefing Document to the Advisory Committee dated October 11, 2013, and at the Advisory Committee meeting itself, the FDA revealed it shared the witness's concern that mineral oil was not inert and stated that it had met with Amarin to discuss the issue in advance of the Advisory Committee hearing. Thus, Defendants knew at the time the REDUCE-IT results became available that any data suggesting concerns with the mineral oil placebo would be important to the public and investors and would need to be made public to avoid creating a misleading perception about the trial's results.

165. In fact, Amarin's 2018 10-K filing formally acknowledged the importance of mineral oil as a placebo in the REDUCE-IT trial as in prior trials:

> "***[D]uring the public advisory committee meeting held by FDA as part of its review of our ANCHOR sNDA, a discussion*** regarding observed, nominally statistically significant changes from baseline in an adverse direction, while on background statin therapy, in certain lipid parameters, including triglycerides, in the placebo group, ***raised questions about the possibility that the mineral oil placebo used in the ANCHOR trial (and in the REDUCE-IT trial) might not be biologically inert and might be viewed as artificially exaggerating the clinical effect of Vascepa when measured against placebo in the ANCHOR trial***. Ultimately, no strong evidence for biological activity of mineral oil was identified by the FDA before its approval of Vascepa after review of the MARINE and ANCHOR trials and consideration of other data regarding mineral oil. … ***Despite the currently positive disposition of this matter, it illustrates that concerns such as this may arise in the future*** that could affect our product development, regulatory review or the public perception of our products and our future prospects.

Amarin 2018 10-K, February 27, 2019 (emphasis added). Yet despite expressly acknowledging the material risk of concerns that the mineral oil may not be inert in the REDUCE-IT trial, when Defendants obtained the results of that trial which bore out those concerns, they concealed those facts during the Class Period and instead presented the misleading results only.

E. SOX Certifications

166. In the Certification Pursuant to Sections 302 and 906 of the Sarbanes-Oxley Act of 2002 he submitted on November 1, 2018, with the Company's Form 10-Q defendant Thero represented that (i) he had reviewed the Company's filing; (ii) the report did "not contain any untrue statement of material fact or omit to state a material fact necessary to make the statements made . . . not misleading"; and (iii) the "information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the [Company]."

167. Thero's possession of the full analyzed REDUCE-IT trial data set, and appreciation of the aberrations in the placebo arm of the data, as described herein, suggests that Thero either was reckless in making his Sarbanes-Oxley certification, or had actual knowledge that the filing did in fact contain untrue statements of material fact or omit to state material facts necessary to make the statements not misleading.

VIII. CLASS ACTION ALLEGATIONS

168. Plaintiffs bring this action as a class action pursuant to Federal Rule of Civil Procedure 23(a) and (b)(3). Plaintiffs bring claims arising under the Exchange Act on behalf of themselves and all other persons and entities who purchased Amarin ADS between September 24, 2018, and November 9, 2018, inclusive, and who were damaged thereby (the "**Class**"). Excluded from this Class are (i) Defendants, (ii) the officers and directors of each Defendant, (iii) any entity in which Defendants have or had a controlling interest, (iv) members of Defendants' immediate families and the legal representatives, heirs, successors or assigns of any such excluded party, and (v) any judge presiding over this matter, his or her spouse, and all persons within the third degree of relationship to either of them and the spouse of such persons.

169. **Numerosity**: The members of the Class are so numerous that joinder of all members is impracticable. While the exact number of Class members is unknown to Plaintiffs at

this time, it can be ascertained through discovery, and Plaintiffs believe that there are thousands of Class members. Throughout the Class Period, the Amarin ADS's at issue traded in an efficient market. Record owners and other members of each Class may be identified from records maintained by Amarin or its transfer agents and may be notified of the pendency of this action by mail, using a form of notice similar to that customarily used in securities class actions.

170. **Commonality and predominance**: Common questions of law and fact exist as to all Class members and predominate over any questions solely affecting individual members of the Class. Common questions include whether:

a. Defendants' acts and omissions violated the Exchange Act;

b. Documents, press releases, and other statements disseminated to the investing public and Amarin's shareholders omitted material facts about Vascepa's REDUCE-IT trial results and the business and financial condition of Amarin;

c. The market price of Amarin's ADS's was artificially inflated due to the material misrepresentations and failures to disclose material facts as described in this Complaint; and

d. Whether members of the Class have sustained damages (and, if so, what the proper measure of damages should be).

171. **Typicality**: Plaintiffs' claims are typical of the claims of the other members of the Class, as all Class members were similarly affected by Defendants' wrongful conduct in violation of federal law.

172. **Adequacy**: Plaintiffs will fairly and adequately protect the interests of the members of the Class because their interests do not conflict with the interests of the members of

the Class the seek to represent. Plaintiffs have retained counsel competent and experienced in class and securities litigation.

173. **Superiority**: A class action is superior to all other available methods for the fair and efficient adjudication of this controversy since joinder of all members is impracticable. Furthermore, as the damages suffered by individual Class members may be relatively small, the expense and burden of individual litigation make it impossible for members of the Class to individually redress the wrongs done to them. Even if Class members themselves could afford such individualized litigation, the court system could not. In addition to the burden and expense of managing many actions arising from this issue, individualized litigation presents a potential for inconsistent or contradictory judgments. Individualized litigation increases the delay and expense to all parties and the court system caused by analyzing and interpreting the legal and factual issues of the case. By contrast, a class action presents far fewer management difficulties and provides the benefits of single adjudication, economies of scale, and comprehensive supervision by a single court. There will be no difficulty in the management of this suit as a class action.

174. In the alternative, the proposed Class may be certified because:

a. The prosecution of separate actions by the individual members of the proposed Class would create a risk of inconsistent adjudications, which could establish incompatible standards of conduct for Defendants;

b. The prosecution of individual actions could result in adjudications that, as a practical matter, would be dispositive of the interests of non-party Class members or which would substantially impair their ability to protect their interests; and

c. Defendants have acted or refused to act on grounds generally applicable to the proposed class, thereby making appropriate final relief with respect to the members of the proposed Class as a whole.

IX. LOSS CAUSATION

175. Amarin and the Officer Defendants' unlawful omissions directly and proximately caused the economic losses sustained by Plaintiffs and Class members.

176. Amarin and the Officer Defendants' omissions caused and maintained the artificial inflation in the Amarin share price throughout the Class Period. When Plaintiffs and Class members purchased their Amarin ADS's, their true value was substantially lower than the prices Plaintiffs and Class members paid. As a result of the open, well-developed, and efficient market for Amarin ADS's, the prices of Amarin ADS's fell when the above-described omissions (and their effects) were revealed to investors and the artificial inflation was removed over time from the price of Amarin shares.

177. Without knowing the misleading nature of the statements and documents discussed, or the undisclosed information known to Defendants, Plaintiffs and Class members relied to their detriment on these statements in purchasing Amarin ADS's at artificially inflated prices during the Class Period.

178. The omissions created in the market an unrealistically positive assessment of Amarin, causing its share prices to be overvalued during the Class Period. Once the facts and risks concealed by Defendants came to light, the price of ADS's dropped, proximately causing damage to Plaintiffs and Class members.

179. Plaintiffs' and Class members' purchases at artificially inflated prices, measured by the difference between the market price and the actual value of the ADS's at the time of purchase, caused damage to Plaintiffs and Class members.

180. The truth regarding Amarin ADS's was revealed, and/or the concealed risks materialized, on or about November 10, 2018. As a direct result of this disclosure, the price of Amarin ADS's declined precipitously on unusually heavy trading volume.

181. On November 10, 2018, Amarin was forced to disclose that their Class Period representations regarding the REDUCE-IT trial omitted material facts about the results, including: (i) the placebo used in the study may have, *inter alia*, raised cholesterol levels in the control arm, which likely exaggerated the clinical effects of Vascepa; and (ii) the Company could not explain the mechanism(s) by which the drug achieved its end-point results.

182. As a direct result of Amarin's admissions and the public revelations on November 10, 2018, regarding the falsity of Amarin and the Officer Defendants' Class Period representations about the REDUCE-IT study, Amarin's share price plummeted 27% on unusually high trading volume, falling from $21.05 to $15.38 in two days.

X. THE FRAUD ON THE MARKET PRESUMPTION

183. Plaintiffs are entitled to a presumption of reliance as to Amarin and the Officer Defendants' material omissions pursuant to the fraud-on-the-market doctrine.

184. As a result of Amarin and the Officer Defendants' materially misleading statements and omissions, Amarin shares traded at artificially inflated prices during the Class Period. On November 5, 2018, Amarin ADS's closed at a Class Period high of $22.98 per share. Plaintiffs and other members of the Class purchased or otherwise acquired the shares relying on the integrity of the market price of such shares and on publicly available market information relating to Amarin; Plaintiffs and Class members have been damaged thereby.

185. During the Class Period, the artificial inflation of the value of Amarin ADS's was caused and sustained by the omissions alleged in this Complaint, thereby causing the damages sustained by Plaintiffs and other Class members. As alleged, during the Class Period, Amarin

and the Officer Defendants' misleading statements and omissions caused the price of Amarin ADS's to be artificially inflated. When the truth was disclosed, it drove down the value of Amarin ADS's, causing Plaintiffs and other Class members that had purchased the shares at artificially inflated prices to be damaged as a result.

186. At all relevant times, the market for Amarin ADS's was open, well-developed, and efficient, for reasons that include:

a. Amarin ADS's met the requirements for listing, and was listed and actively traded on the NASDAQ Global Market, a highly efficient and automated market;

b. As a regulated issuer, Amarin filed periodic public reports with the SEC;

c. Amarin regularly and publicly communicated with investors via established market communication mechanisms, including through regular disseminations of press releases on the national circuits of major newswire services and through other wide-ranging public disclosures, such as communications with the final press and other similar reporting services; and

d. Amarin was followed by securities analysts employed by major brokerage firm(s) who wrote reports which were distributed to the sales force and certain customers of their respective brokerage firm(s). Each of these reports was publicly available and entered the public marketplace.

187. As a result of the foregoing, the market for Amarin ADS's promptly digested current information regarding Amarin from all publicly available sources and reflected such information in the inflated price of Amarin ADS's during the Class Period. Under these circumstances, all members of the Class suffered similar injury through their purchase of Amarin ADS's at artificially inflated prices on which they relied, and the presumption of reliance applies.

188. In the alternative, a class-wide presumption of reliance is also appropriate in this action under the Supreme Court's holding in *Affiliated Ute Citizens of Utah v. United States*, 406 U.S. 128 (1972), to the extent that Amarin and the Officer Defendants' statements during the Class Period involved omissions of material facts.

189. Because this action involves Amarin and the Officer Defendants' failure to disclose material adverse information regarding the REDUCE-IT trial results, including that the mineral oil placebo caused aberrations in the placebo arm, likely exaggerating the clinical efficacy of Vascepa, and that the Company could not be explained the mechanism by which the drug achieved its end-point results—information that Amarin and the Officer Defendants were obligated to disclose—positive proof of reliance is not a prerequisite to recovery.

190. All that is necessary is that the facts withheld be material in the sense that a reasonable investor would have considered them important in making investment decisions. Given the importance of the REDUCE-IT trial and its results to Amarin's overall financial prospects, that requirement is satisfied here.

XI. NO STATUTORY SAFE HARBOR

191. The statutory safe harbor or bespeaks caution doctrine applicable to forward-looking statements under certain circumstances do not apply to any of the false and misleading statements pleaded in this Complaint. None of the statements complained of was a forward-looking statement. Rather, they were historical statements or statements of purportedly current facts and conditions at the time the statements were made, including statements about the nature of Amarin's REDUCE-IT Vascepa results and the viability of its Vascepa drug. Moreover, the statutory safe harbor does not apply to statements included in financial statements that purport to have been prepared in accordance with GAAP.

192. To the extent that any of the misleading statements alleged herein can be construed as forward-looking, those statements were not accompanied by meaningful cautionary language identifying important facts that could cause actual results to differ materially from those in the statements. As detailed above, then-existing facts contradicted Amarin and the Officer Defendants' statements regarding the nature of the REDUCE-IT trial results and the viability of its Vascepa drug, among others. Given the then-existing facts contradicting Amarin and the Officer Defendants' statements, any generalized risk disclosures made by Amarin were not sufficient to insulate them from liability for their materially false and misleading statements. Further, any cautionary language was not extensive, specific, or directly related to the false and misleading statements alleged.

193. To the extent that any misleading statements pleaded herein are forward-looking, Amarin and the Officer Defendants are liable for those statements because at the time each of those statements was made, the particular speaker knew the particular forward-looking statement was misleading, and the misleading forward-looking statement was authorized and approved by an executive officer of Amarin who knew that the statement was misleading when made. As described above, these misleading statements were material to investors. Amarin and the Officer Defendants did not identify each oral or written statement identified as forward-looking.

XII. CAUSES OF ACTION

FIRST COUNT
Violation of Section 10(b) of The Exchange Act and Rule 10b-5 Promulgated Thereunder Against Amarin and the Officer Defendants

194. Plaintiffs repeat and reallege the allegations set forth above.

195. Plaintiffs assert this claim against Amarin and the Officer Defendants on behalf of Plaintiffs and the proposed Class.

196. Amarin and the Officer Defendants individually or in concert, by the use of means or instrumentalities of interstate commerce and/or of the United States mail: (1) employed devices, schemes, and artifices to defraud; (2) made untrue statements of material fact and omitted material facts; (3) deceived the investing public, including Plaintiffs and Class members; (4) artificially inflated and maintained the market price of Amarin ADS's; and (5) caused Plaintiffs and Class members to purchase Amarin shares at artificially inflated prices and suffer losses. Amarin and the Officer Defendants were primary participants in this wrongful and illegal conduct.

197. The Officer Defendants were top officers and controlling persons of Amarin and had direct involvement in its day-to-day operations. They were high level executives or directors at Amarin during the Class Period such that they managed or controlled the management of the company. Each of the Officer Defendants, by virtue of their responsibilities and activities as a senior officer or director, was involved in publication of Amarin's documents attributed to them in Section V above. The Officer Defendants were involved in drafting, producing, reviewing, or disseminating the documents at issue in this action. Each Officer Defendant enjoyed significant personal contact and familiarity with the other Defendants and were advised of, and had access to, other members of the management team, internal reports, and other data and information at all relevant times. Each Officer Defendant was aware of the Company's dissemination of information to the investing public which they knew or recklessly disregarded was materially misleading.

198. Amarin and the Officer Defendants knew, or were reckless in not knowing, of the material misrepresentations and omissions described in this Complaint or acted with reckless disregard for the truth in that they failed to ascertain and to disclose such facts, even though such

facts were readily available to them. The Officer Defendants' material misrepresentations and omissions were done knowingly or recklessly and for the purpose and effect of concealing the REDUCE-IT trial's full results and Amarin's financial condition and results of operations, business practices, and future business prospects from the investing public and supporting the artificially inflated price of its ADS's.

199. As a result of this dissemination of the materially misleading statements and omissions, the market price of Amarin shares was artificially inflated during the Class Period. In ignorance of the fact that market prices of Amarin shares were artificially inflated, and relying upon the integrity of the market in which the ADS's trade, and in the absence of material adverse information that was known to or recklessly disregarded by Defendants, but not disclosed in public statements by Amarin and the Officer Defendants during the Class Period, Plaintiffs' and the other members of the Class acquired Amarin ADS's during the Class Period at artificially high prices and were damaged thereby.

200. At the time of the misrepresentations and omissions, Plaintiffs and other members of the proposed Class were ignorant of their falsity. Had Plaintiffs and the other members of the Class and the marketplace known that Amarin's share prices were artificially inflated, Plaintiffs and other members of the proposed Class would not have purchased or otherwise acquired their Amarin ADS's, or, if they had acquired such ADS's during the Class Period, they would not have done so at the artificially inflated prices which they paid.

201. By virtue of the foregoing, Amarin and the Officer Defendants each violated Section 10(b) of the Exchange Act and Rule 10b-5 promulgated thereunder.

202. This claim was brought within two years after the discovery of the fraud and within five years of the making of the materially false and misleading statements alleged.

203. As a direct and proximate result of Amarin and the Officer Defendants' wrongful conduct, Plaintiffs and Class members suffered damages in connection with their transactions of Amarin ADS's.

SECOND COUNT
Violation of Section 20(a) of the Exchange Act
Against the Individual Defendants

204. Plaintiffs repeat and reallege the allegations set forth above.

205. This claim is asserted against the Individual Defendants on behalf of Plaintiffs and proposed Class members.

206. The Individual Defendants were and acted as controlling persons of Amarin within the meaning of Section 20(a). By virtue of their high-level positions with Amarin, participation in and awareness of Amarin's operations, direct involvement in the day-to-day operations of Amarin, and intimate knowledge of Amarin's actual performance, the Individual Defendants had the power to influence and control, and did influence and control, Amarin's decision-making, including the content and dissemination of the statements that Plaintiffs contend are false and misleading as set forth in Section V above. The Individual Defendants had direct and supervisory involvement in the day-to-day operations of Amarin and, therefore, are presumed to have had the power to control or influence the particular transactions giving rise to the securities violations as alleged herein, and exercised the same, and thus were culpable participants in Amarin and the Officer Defendants' fraud.

207. As set forth above, Amarin and the Officer Defendants each violated Section 10(b) and Rule 10b-5 by their acts and omissions detailed above. By virtue of their positions as controlling persons, the Individual Defendants are liable pursuant to Section 20(a) of the Exchange Act.

208. As a direct and proximate result of Individual Defendants' wrongful conduct, Plaintiffs and proposed Class members suffered damages in connection with their acquisition of Amarin ADS's during the Class Period.

XIII. PRAYER FOR RELIEF

209. Plaintiffs, on their own behalf and on behalf of the Class, pray for judgment as follows:

a. Declaring this action to be a class action pursuant to Federal Rule of Civil Procedure 23(a) and (b)(3);

b. Awarding Plaintiffs and the other members of the Class damages in an amount which may be proven at trial, together with interest thereon;

c. Awarding Plaintiffs and members of the Class pre-judgment and post-judgment interest, as well as their reasonable attorneys' and expert witness' fees and other costs;

d. Awarding Plaintiffs and the members of the Class rescission and/or rescissory damages; and

e. Such other relief as this Court deems appropriate.

XIV. JURY TRIAL DEMAND

Plaintiffs hereby demand a trial by jury.

Dated: July 22, 2019

Respectfully Submitted,

By: */s/ Sherief Morsy*
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Plaintiffs' Counsel

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on July 22, 2019, I caused true and correct copies of the foregoing to be served on all counsel of record via CM/ECF.

Dated: July 22, 2019

By: /s/ *Sherief Morsy*
Sherief Morsy (#125042015)